COMPARING EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POST OPERATIVE ANALGESIA – A DOUBLE BLINDED RANDOMIZED STUDY

Dissertation submitted

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CERTIFICATE

This is to certify that this dissertation titled **"COMPARING EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POST OPERATIVE ANALGESIA – A DOUBLE BLINDED RANDOMIZED STUDY"** has been prepared by Dr. J.SURESH under my supervision in the Department of Anesthesiology, Government Kilpauk Medical College, Chennai during the academic period 2010-2013 and is being submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the University regulation for the award of Degree of Doctor of Medicine (M.D Anesthesiology) and his dissertation is a bonafide work.

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DECLARATION

I, Dr. J. Suresh solemnly declare that the dissertation,"**COMPARING EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POST OPERATIVE ANALGESIA – A DOUBLE BLINDED RANDOMIZED STUDY"** is a bonafide work done by me in the Department of Anesthesiology and Critical care, Government Kilpauk Medical College& Hospital, Chennai under the guidance of **Prof.S.Gunasekaran,** M.D.,D.A,.D.N.B., Professor and HOD, Department of Anesthesiology, Government Kilpauk Medical College, Chennai-10.

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CONTENTS

1. INTRODUCTION

The perioperative period is usually associated with a variety of pathophysiologic responses that are initiated or maintained by nociceptive input. Uncontrolled postoperative pain may produce various acute and chronic effects which may be detrimental to the patient.

The perioperative pathophysiological changes that occurs during surgery can be attenuated through reduction of transmission of nociceptive input to the central nervous system by providing perioperative analgesia. This also

- Decreases complications,

-Facilitate recovery during the immediate postoperative period,

-Improves long term recovery,

-Reduces the length of hospital stay,

-Improves the quality of life.[1]

Post operative pain management should be planned and tailored to the needs of special population like ambulatory surgical patient, elderly, paediatric, opioid tolerant, obese patients and those with obstructive sleep apnea syndrome.

IMMEDIATE EFFECTS OF POSTOPERATIVE PAIN:

Transmission of nociceptive stimuli from the periphery to the Central nervous system results in the neuroendocrine stress response, a combination of local inflammatory substances (eg.cytokines, prostaglandins, leukotrienes, tumor necrosis factor-α) and systemic mediators of the neuroendocrine response.

Suprasegmental reflex response to pain results in increased sympathetic tone, increased catecholamine levels, increased catabolic hormone secretion and decreased secretion of anabolic hormones which results in sodium and water retention , increased levels of blood glucose, free fatty acids, ketone bodies and lactate.

A hypermetabolic state occurs as metabolism and oxygen consumption are increased. The extent of the stress response is influenced by following factors:

- the type of anesthesia,
- the degree of surgical trauma.

The stress response may lead to postoperative hypercoagulability. Enhancement of coagulation, inhibition of fibrinolysis, increased platelet reactivity and plasma viscosity may contribute to an increased incidence of postoperative hypercoagulablility related events such as deep venous thrombosis, vascular graft failure and myocardial ischemia. The stress response

also potentiate postoperative immunosuppression, the extent of which correlates with the severity of surgical injury.

Sympathetic activation may increase myocardial oxygen consumption, decrease myocardial oxygen supply through coronary vasoconstriction and attenuation of local metabolic coronary vasodilation.

Activation of the sympathetic nervous system also delays return of postoperative gastrointestinal motility, which may develop into paralytic ileus[(2)]

Postoperative respiratory function is markedly decreased, especially after upper abdominal and thoracic surgery. Reflex inhibition of phrenic nerve activity is an important component of this decreased postoperative pulmonary function. Patients with poor pain control may breathe less deeply, have an inadequate cough, and more susceptible to the development of postoperative pulmonary complications.

DELAYED EFFECTS OF POSTOPERATIVE PAIN:

Chronic postsurgical pain [CPSP] is a largely unrecognized problem that may occur in 10% to 65% of postoperative patients. Poorly controlled acute postoperative pain may be an important predictive factor in the development of CPSP. The transition from acute to chronic pain occurs very quickly and longterm behavioral and neurobiologic changes occur much earlier than was previously thought.

CPSP is relatively common after procedures such as limb amputation (30% to 83%), thoracotomy (22% to 67%), sternotomy (10 to 27%), and breast surgery (11% to 57%).

Traditionally various techniques and drugs have been adopted for postoperative analgesia. These include regional techniques like epidural analgesia with local anesthetics alone or opioid alone or combination of both, peripheral blocks, NSAIDS, parenteral opioids, non epidural analgesia like intrapleural analgesia, paravertebral block, intra articular analgesia etc.

Epidural steroids have been used successfully for long time for chronic pain syndrome. The safety of epidural steroids is well established. Based on the above evidences and concepts in this study we used dexamethasone epidurally to study the effects on acute postoperative pain.

HISTORY OF EPIDURAL ANESTHESIA & ANALGESIA

- Jean Enthuse Sicard (1872-1929) and Fernand Cathelin (1873-1945) independently introduced cocaine through the sacral hiatus in 1901 ,thereby becoming the first practitioners of caudal (epidural) anesthesia.
- Sicard - a neurologist, used the technique to treat sciatica and tabes, but Cathelin used the technique for surgical anesthesia.
- Arthur Läwen (1876-1958)- an early proponent of regional anesthesia, successfully used caudal anesthesia with large volumes of procaine for pelvic surgery.
- Heile - published an extensive study of the epidural space in 1913. His unique approach was to enter the epidural space through the intervertebral foramina.
- In 1921, Fidel Pagés (1886-1923), a Spanish military surgeon- devised a technique to introduce epidural procaine at all levels of the neuraxis. His method was to use a blunt needle and then feel and hear entry of the needle through the ligamentum flavum.
- An important innovation was Dogliotti's method of identification of the epidural space. His textbook illustrates the use of continuous pressure on the plunger of a saline filled syringe as the needle is advanced through the ligamentous structures.

- Gutierrez of Argentina developed the “hanging drop” sign, which is still used by some anesthesiologists to identify the epidural space. William T. Lemmon (1896-1974) used a 17-gauge, malleable, silver needle that was connected through a hole in the operating room table to rubber tubing and a syringe.
- Edward B. Tuohy (1908-1959) used a ureteral catheter threaded through a large Huber-tipped spinal needle to provide continuous spinal anesthesia.
- Behar in 1979 first reported the use of epidural morphine for treatment of pain.
- Robecchi and Capra in 1952 treated radiculopathy with periradicular hydrocortisone. It is the first documented use of epidural steroids .

2. ANATOMY OF EPIDURAL SPACE

Everything outside the dural sac but within the vertebral canal can be considered to constitute the epidural space.

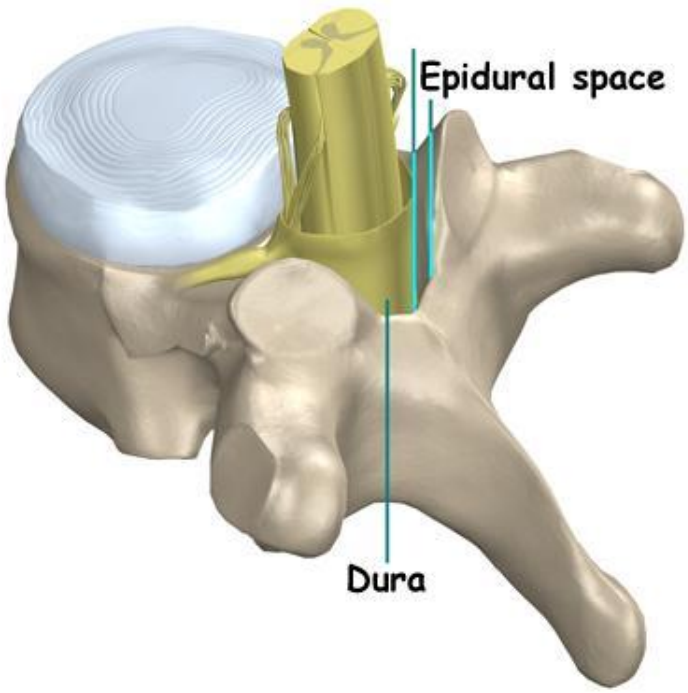
Boundaries of epidural space:

- The walls of vertebral canal including the vertebral bodies and discs anteriorly
- Pedicles laterally
- Lamina and ligamentum flava posteriorly

Epidural space is a potential space normally contains – fat, vessels and nerves. The cranial epidural space is entirely empty. The epidural fat which is nearly fluid in texture permits gliding movement of the neural structures and provides a padding effect. The distribution of epidural contents is highly non uniform.

Separated by these empty areas, the epidural contents occur as a series of metamerically and circumferentially discontinuous compartments. In contrast to this below L4, the dural sac tapers resulting in complete filling of epidural fat. Thus there will be difficulty in delivering local anaesthetic to the L5 and sacral nerve roots during epidural anaesthesia, since solution is not confined in close

proximity with neural structures at these levels.



Posterior epidural compartment:

A triangular part of fat pad fills the dura posterior to epidural space. It is enclosed by ligamentum flava but also extends under the caudal most portion of lamina above. The largest posterior epidural compartment is at the mid lumbar level with progressive decrease in anteroposterior dimension at thoracic levels[(3)]. Rostral to C7 level the posterior epidural space vanishes and the posterior dura lies in contact with the ligamentum flavum and the laminar bone.

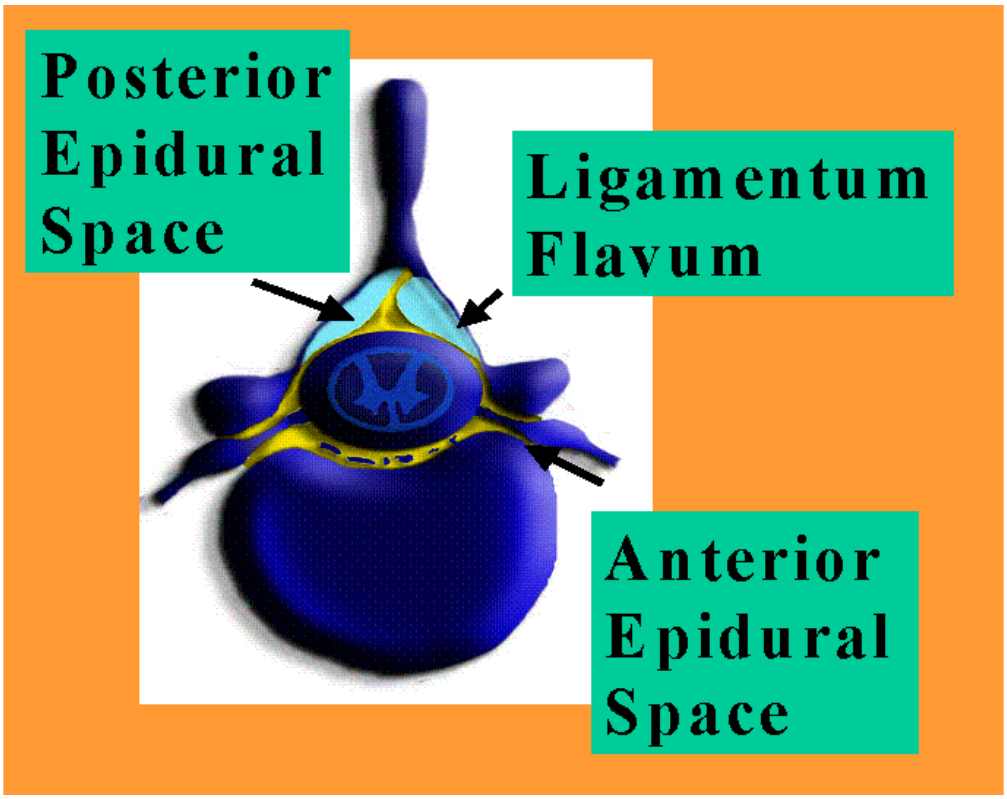
A cleft like space between epidural fat and the canal wall allows passage of catheters and injected fluids with only a minor impediment in posterior midline. This arrangement of opposing non adherent tissue plane is ideally designed to demonstrate the normal subatmospheric pressure within tissues, generated by

the usual action of lymphatics and the balance of osmotic and hydrostatic forces across the capillary endothelium.

Lateral epidural compartment:

No epidural contents exist lateral to the dural sac where it is in contact with the vertebral pedicles. This compartment forms just medial to each intervertebral foramen and is filled with segmental nerves, vessels and fat.

The pressure in the epidural space closely reflects abdominal pressure because of the flexibility of tissues and lack of rigid barrier. Increased abdominal pressure such as during a cough or pregnancy is therefore readily transmitted to the epidural space.



Anterior epidural space:

The anterior epidural compartment is separated from rest of vertebral column by fascia of posterior longitudinal ligament. The spread of injected drug anterior to plane of posterior longitudinal ligament is effectively blocked by this membrane.At the level of the narrow mid portion of the vertebral body this is almost occupied by internal vertebral plexus. Catheters that transgress into the anterior epidural space through the fascia of the posterior longitudinal ligament are likely to enter the venous plexus.

Functional implications of epidural space:

The spread of injected solutions is circumferential at a given level and passes out of the intervertebral foramen and likewise freely passes longitudinally within the vertebral canal.

As the catheter is advanced through the needle, there may be a brief resistance to advancement as the tip encounters the dura. CT scan shows that catheter tip inserted 3 cm into the vertebral canal most commonly travel laterally to the internal aspect of an intervertebral foramen because of the stiffness of the short segment of catheter that has emerged from the needle. Even when the catheter tip lies exterior to the intervertebral foramina in the paravertebral space, the distribution of the injected solution is preferentially back into the vertebral canal .

PHYSIOLOGICAL EFFECTS OF EPIDURAL BLOCKADE

Epidural neural blockade implies sympathetic blockade accompanied by somatic blockade in the form of sensory and motor blockade alone or in combination.

CARDIOVASCULAR EFFECTS:

Blockade of sympathetic innervation accounts for the cardiovascular responses. Preganglionic sympathetic innervation – regulates regional blood flow. Post ganglionic sympathetic innervations – controls cardiac function and vascular tone. Peripheral sympathetic blockade causes vascular dilatation in pelvis and lower limbs when lower thoracic and lumbar segments are blocked with epidural anaesthesia.

Cardiovascular depression is atleast partly related to the level of sympathetic blockade. Vascular absorption of local anaesthetic and addition of vasoconstrictor may result in significant hemodynamic changes after epidural but not after subarachnoid blockade.

Lumbar epidural anaesthesia with sympathetic blockade below T10 results in minimal vasodilatory consequences because fewer vasoconstrictor fibres are included and neither the sphlanchnic nerves nor the nerve supply to the adrenal medulla are affected. Since muscle veins lack sympathetic innervation, venodilatation of the extremities is limited to skin and so minimal capacitance

increase results from blocks of the lower extremities.[4] Lumbar epidural anesthesia with a sympathetic blockade extending to the lower segments may occasionally be associated with profound bradycardia and circulatory collapse without any obvious precipitating event.

RESPIRATORY EFFECTS:

Following aspects may influence respiration.

- sensory neural blockade reduces nociceptive afferent drive to respiratory center.
- motor neural blockade of intercostals muscles, abdominal muscles and diaphragm.
- sympathetic neural blockade with resultant change in cardiac output .
- vagal dominance.

The potential for phrenic nerve palsy is rare with epidural block. Respiratory arrest is rare and commonly associated with extensive sympathetic blockade, reduced cardiac output and reduced oxygen to the CNS. In patients with severe pain epidural block probably improves Vital capacity and Functional residual capacity as well as PaO2. Thoracic epidural anesthesia does not impair the hypoxic drive. The inhibitory reflex of phrenic nerve motor drive is interrupted with thoracic epidural anesthesia resulting in increased diaphragmatic activity .

NEUROENDOCRINE EFFECTS OF EPIDURAL BLOCKADE:

Most of the surgically induced endocrine and metabolic changes are abolished by an appropriate level of sensory blockade produced by regional anesthesia. Surgical stress responses during major upper abdominal and thoracic procedures are not effectively amileorated by epidural anaesthesia due to incomplete blockade of nociceptive pathways. Sympathetic block abolishes the increase in renin activity in response to arterial hypotension. Vasopressin system is activated in response to hypotension

EPIDURAL BLOCKADE AND MOTOR FUNCTION:

The degree of motor blockade increases as dose of drug increases. Usage of dilute concentration of local anesthetics facilitates ultra early ambulation. Motor blockade in lower limbs is assessed by bromage scale.

BROMAGE SCALE:

No block (0%)	Full flexion of knees and feet possible
Partial (33%)	Just able to flex knees, still full flexion of feet possible
Almost complete(66%)	Unable to flex knees, still flexion of feet
Complete (100%)	Unable to move legs or feet

Table 1 showing assessment of motor blockade in lower limb

RECTUS ABDOMINIS MUSCLE (RAM) TEST:

This is useful in abdominal surgery, when abdominal muscle blockade is required rather than lower limb muscle blockade.[5]

100% power	Able to rise from supine to sitting position with hands behind head
80% power	Can sit only with arms extended
60% power	Can lift only head and scapula off bed
40% power	Can lift only shoulders off bed
20% power	An increase in abdominal muscle tension can be felt during effort; no other response

Table 2 showing assessment of motor blockade of abdominal muscles.

THERMOREGULATION AND SHIVERING:

Hypothermia is common in patients undergoing surgery with epidural anesthesia and it results from heat loss to the cold environment due to sympathectomy induced vasodilatation and in part from redistribution of heat from central to peripheral regions.

Pregnancy may enhance the contribution of spinal thermoregulatory input. Injection of epidural pethidine 25mg or epidural fentanyl 50 µg abolishes shivering from epidural local analgesia.

EFFECTS ON GIT:

Epidural block extending from T6 to L1 effectively denervates the sphlanchnic sympathetic supply to the abdominal viscera. As a result parasympathetic activity predominates resulting in contraction of gut. Thoracic epidural anesthesia with local anaesthetics shortens the duration of postoperative paralytic ileus. Unopposed parasympathetic activity with blockade of afferent nociceptive and thoracolumbar efferents produces a shortened postoperative colonic ileus.

Epidural anesthesia have protective action on gut due to improved mucosal blood flow. This increase in blood flow may contribute to the healing of gut anastomosis. Epidural anesthesia with local anaesthetic seems to be the best method for relieving pain after gastrointestinal surgery.

EFFECTS ON BLOOD LOSS:

Patients receiving epidural block had operative blood losses that were half those associated with general anaesthesia. Blood loss can be reduced as far as

30 to 40 % if epidural block is used for hip surgery. Factors that reduce blood loss include mild reduction in arterial blood pressure, increase in venous capacitance, prevention of high venous pressure in response to sympathetic activity resulting from pain and use of appropriate position.

EPIDURAL ANESTHESIA & ANALGESIA

Epidural anesthesia is a central neuraxial block technique which provides segmental blockade. Improvements in equipment, drugs and technique have made it a popular and versatile anesthetic technique, with applications in surgery, obstetrics and pain control. Its versatility means it can be used as an anesthetic, as an analgesic adjuvant to general anesthesia, and for postoperative analgesia in procedures involving the lower limbs, perineum, pelvis, abdomen and thorax.

General indications:

Epidural anesthesia can be used as sole anesthetic for procedures involving the lower limbs, pelvis, perineum and lower abdomen. It is possible to perform upper abdominal and thoracic procedures under epidural anesthesia alone, but the height of block required, with its attendant side effects, make it difficult to avoid significant patient discomfort and risk.

The advantage of epidural over spinal anesthesia is the ability to maintain continuous anesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration. This feature also enables the use of this technique into the postoperative period for analgesia, using lower concentrations of local anaesthetic drugs or in combination with different agents.

Specific indications:

Hip and knee surgery: Internal fixation of a fractured hip is associated with less blood loss when central neuraxial block is used. The rate of deep venous thrombosis is reduced in patients undergoing total hip and knee replacement, when epidural anaesthesia is used.

Vascular reconstruction of the lower limbs: Epidural anesthesia improves distal blood flow in patients undergoing arterial reconstruction surgery.

Amputation: Patients given epidural anaesthesia 48-72 hours prior to lower limb amputation may have a lower incidence of phantom limb pain following surgery.

Thoracic trauma with rib or sternum fractures: Adequate analgesia in patients with thoracic trauma improves respiratory function by allowing the patient to breathe adequately, cough and cooperate with chest physiotherapy.

Obstetrics: Epidural analgesia is indicated in obstetric patients in difficult or high-risk labour.Caesarean section performed under central neuraxial block is associated with a lower maternal mortality and better perioperative outcome.

CONTRAINDICATION OF EPIDURAL ANESTHESIA:

ABSOLUTE:

- Patient refusal

- Infection at the site of injection
- Coagulopathy or other bleeding diathesis
- Severe hypovolemia
- Increased intracranial pressure
- Severe stenotic valvular heart disease with low fixed cardiac output syndrome.
- Severe hypotension
- Known allergy to local anesthetics

RELATIVE:

- Sepsis
- Uncooperative patient
- Pre-existing neurological disease
- Severe spinal deformities
- Patients on anticoagulants.

ADVANTAGES:

- Use of perioperative epidural anesthesia and analgesia, especially with a local anesthetic–based analgesic solution, can attenuate the pathophysiologic response to surgery and may be associated with a reduction in mortality and morbidity when compared with analgesia with systemic opioid agents. Use of epidural analgesia can decrease the

incidence of postoperative gastrointestinal, pulmonary, and possibly cardiac complications by inhibiting sympathetic outflow, decreasing the total opioid dose, and attenuating spinal reflex inhibition of the gastrointestinal tract.

- Postoperative thoracic epidural analgesia can facilitate return of gastrointestinal motility without contributing to anastomotic bowel dehiscence. Patients who receive epidural local anesthetics have an earlier return of gastrointestinal motility after abdominal surgery.
- Perioperative use of epidural analgesia with a local anesthetic–based regimen in patients undergoing abdominal and thoracic surgery decreases postoperative pulmonary complications, presumably by preserving postoperative pulmonary function by providing superior analgesia and thus reducing splinting behavior and attenuating the spinal reflex inhibition of diaphragmatic function.

- Use of postoperative thoracic, but not lumbar epidural analgesia may decrease the incidence of postoperative myocardial infarction[(12)],possibly by attenuating the stress response hypercoagulability, improving postoperative analgesia and providing favorable redistribution of coronary blood flow.

FACTORS AFFECTING EPIDURAL BLOCKADE:

SITE OF INJECTION AND NERVE ROOT SIZE:

Injection of drug close to nerve roots results in rapid and intense blockade. After lumbar epidural injection, a somewhat greater cranial than caudal spread of analgesia occurs. The spread of analgesia is even when drugs are injected in midthoracic epidural injection.

Concentration of large number of nerve fibres within upper thoracic and cervical segments makes them resistant to blockade with epidural injections. Caudal epidural block spreads from S5 and the S1 segment is the last to be blocked.

VOLUME:

Segmental dose is the spread of the volume of anesthetic solution injected in ml per no of dermatomes blocked. The capacity of lower part of epidural space is larger. For each pair of segment the following dose is recommended:

For cervical region – 1.5 ml

For thoracic region – 2 ml

For lumbar region - 2.5 ml

The per segment volume of anesthetic solution necessary in sacral and lower lumbar region is greater. For single injection technique the dose should range

from 15 – 20 ml of anesthetic solution. For continous technique the initial dose is 8 – 12 ml and subsequently 5 – 7 ml every hour.

AGE:

In the elderly, the areolar tissue around the intervertebral foramina becomes dense and firm partially sealing the foramina. The permeability of duramater increases with increase in age. Aging is associated with reduced beta adrenergic responsiveness. Increased levels of analgesia with increase in age is due :

- Progressive sclerosis of intervertebral foramina results in reduced leakage of injected solutions into paravertebral space.
- Increased permeability of duramater.
- Increased compliance of the epidural space.
- Decreased resistance of epidural space.

With aging neural population declines steadily within the spinal cord and peripheral nerves show a linear reduction in conduction velocity especially motor nerves. These changes makes older patients more sensitive to local anesthetics with altered motor block profile.

Thermoregulatory response declines with age as shown by decrease in core temperature consequently rewarming process will occur more slowly in elder patients.

CONCENTRATION AND DOSE OF LOCAL ANAESTHETIC:

Below concentrations of 1% lignocaine motor block is minimal regardless of dose, unless injections are repeated at intervals. When dilute solutions in concentration of 0.125% or 0.625% bupivacaine are injected repeatedly the intensity of sensory and motor blockade increase. This mechanism is particularly important in obstetric analgesia. Increasing concentration results in reduction in onset time yet produces intense motor blockade.

DRUG	CLINICAL USE	CONCENTRATION (%)	DURATION(min)
Lignocaine	infiltration	0.5	60 - 240
	Peripheral blocks	1	60 – 200
	epidural	1.5 - 2	60 - 120
	spinal	2 - 5	30 - 60
Bupivacaine	infiltration	0.25	120 - 480
	epidural	0.5	120 - 300
	spinal	0.5	60 - 240
Ropivacaine	infiltration	0.2 – 0.5	120 - 360
	epidural	0.5 - 1	120 - 360
	spinal	0.5 – 0.75	90 - 200

Table 3 showing concentration of commonly used drugs.

If more potent analgesia with minimal motor block is required 0.5% bupivacaine, 0.5% ropivacaine, 0.5% levobupivacaine or 1% lignocaine may be chosen. The requirement of profound sensory block and excellent muscle relaxation are best met by 1% lignocaine with epinephrine or 0.75% to 1% ropivacaine. The toxic plasma concentration of lignocaine, bupivacaine, ropivacaine were >5, > 3, >4 ng / ml respectively.

POSITION OF THE PATIENT:

Comparison of sitting and lateral position for epidural block reveals no significant differences in cephalad spread. An exception is the obese patient who achieves a lower level of block when seated. The spread of analgesia is more intense in dependent portion when drugs injected in lateral position in both pregnant and non pregnant women. Motor and sensory block onset will be rapid in the dependent portion.

SPEED OF INJECTION:

Rapid injection of local anesthetics into epidural space has no effect on spread of analgesia and has only minimal effect on bulk flow of solution in the space. Rapid injections of large volumes of solution may increase CSF pressure, decreases spinal cord blood flow, increase intracranial pressure and pose a risk of spinal or cerebral complications. Headache is commonly reported if epidural solutions are rapidly injected.

NUMBER & FREQUENCY OF LOCAL ANESTHETIC INJECTIONS:

A single repeat dose (20% of total dose) given approximately 20 minutes after the main dose of local anaesthetic has been said to consolidate blockade within the level of blockade already established. Thus missed segments may be filled in but the level of blockade may not be extended. A second dose of approximately 50% of initial dosage will maintain the initial segmental level of analgesia if given when the upper level of segmental analgesia has receded 1 to 2 dermatomes. In addition tachyphylaxis increases with the number of injections especially when short acting amides are used.

ADJUVANTS:

EPINEPHRINE:

When freshly prepared epinephrine in a concentration of 1:2,00,000 is added to the local anaesthetic solution , it

- Improves the quality of sensory block.
- Increases the duration and intensity of motor blockade.

Enhancement of analgesia seen with epinephrine is due to activation of dorsal horn inhibitory system via α 2 adreno receptor and to some extent through decreased vascular absorption.

CLONIDINE:

It is a selective α 2 adrenergic agonist which acts by opening potassium channels. Prolongs duration of both sensory and motor blockade by synergistic action with local anaesthetics.

Side effects:

- Arterial hypotension- due to direct inhibition of sympathetic outflow from pre ganglionic neurons in the spinal cord,
- reduction in heart rate .

KETAMINE:

It blocks the calcium channel on the NMDA (N- methyl D aspartate) receptor complex and decreases depolarisation by inhibiting excitatory transmission.

NEOSTIGMINE:

The cholinergic system modulates pain perception by a spinal mechanism. Analgesia by neostigmine is associated with high incidence of nausea and vomiting.

3. PHYSIOLOGY OF PAIN

PAIN:

International association for study of pain has defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or defined in terms of such damage.

There are two components of pain. Neurophysiologically mediated sensory component and an emotional component.

There are two types of pain

1. Physiological pain is a transient sensation due to noxious mechanical, thermal, chemical stimulus each with a clearly defined threshold and without causing damage to the nervous system.
2. Pathological pain is an inflammatory response to tissue injury or damage to central nervous system with an alteration in perception. Pain following surgery is pathological.

There are two major theories of pain.

1. Specificity theory proposed by Von Frey states that pain is due to stimulation of specific end organs.
2. Intensive / Summation / Pattern theory proposed by Gold Scheider states that there are no specific pain receptors and any sensory stimulus if sufficiently severe would produce pain.

ORGANISATION OF PAIN PATHWAYS:

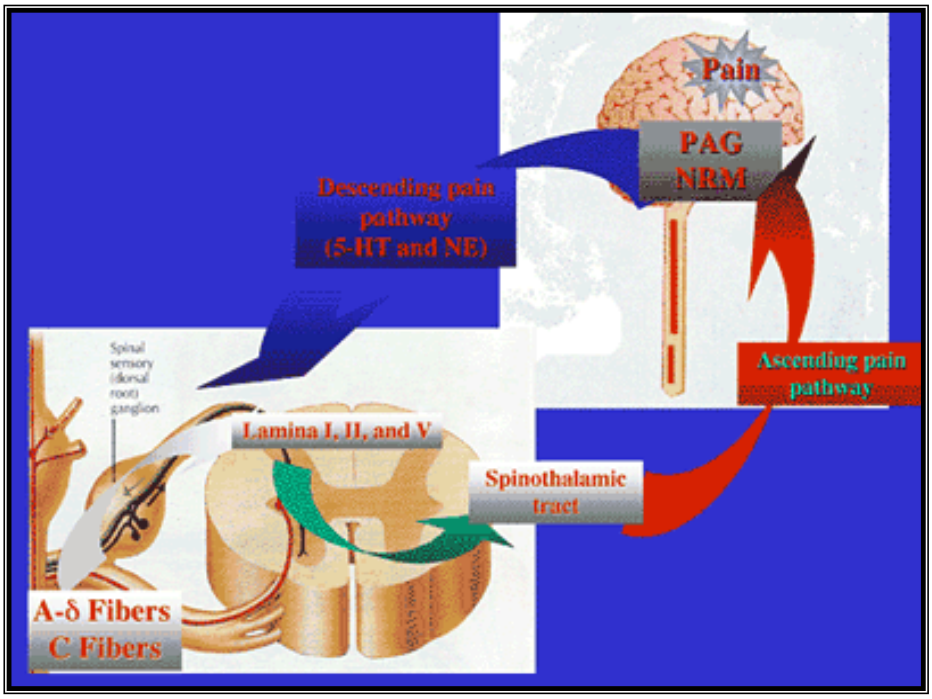
According to the recent theory, pain pathway is organized as follows

RECEPTORS:

Nociceptive receptors are fine, profusely branched, free nerve endings covered by Schwann cells with little or no myelin. They are present in skin, viscera and other organs.

There are three types of receptors

1. Mechanosensitive nociceptors activated by mechanical stimuli.
2. Mechanothermal nociceptors activated by mechanical and thermal stimuli >43ºC.
3. Polymodal pain receptors respond to mechanical, thermal and chemical stimuli like hydrogen, potassium ions, histamine, serotonin, prostaglandins.



FIRST ORDER NEURONS:

Mechanosensitive and mechanothermal pain receptors transmit impulses through thinly myelinated A δ fibres of 1-5 µ diameter with conduction velocity of 15-30 metres per second. This is responsible for fast pain which is sharply localized. Polymodal pain receptors transmit impulses through unmyelinated C fibres of 0.4-1.1 µ diameter with conduction velocity of 0.5 – 2 meters per second. This is responsible for the poorly localized slow pain. Transmission through both these fibres causes the " Double response of Lewis". The peripheral afferent fibres have their cell body in the dorsal root ganglion and project via the lateral part of the dorsal root called " Tract of Lissauer". They terminate in dorsal horn of spinal cord within 1 to 2 segments of entry. A δ fibres terminate in lamina 1 (marginal cell layer of Waldeyer) and lamina 5 (wide dynamic range of neurons which respond to other modalities also). Unmyelinated C fibres terminate in lamina 2 and 3 (substantia gelatinosa).

SECOND ORDER NEURONS:

They arise from the cell and connect with ventral and lateral horn cells in the same and adjacent spinal segments which subserve both somatic and autonomic reflexes. Around 75% of other sensory neurons project contralaterally after decussating in the anterior commissure 1-3 segments higher than the root of entry and divide into two ascending tracts.

Neospinothalamic / Lateral spinothalamic tract:

It ascends in the anterolateral funiculus of spinal cord to brain stem and thalamus. It contains fast conducting fibres which transmit specific localised pain, identifiable in quality and intensity causing “First Pain “. The fibres are arranged in such a way that fibres from lower part of the body are superficial and from upper part of the body are innermost.

Palaeospinothalamic / Ventral spinothalamic / Spinoreticulothalamic tract:

It is medially placed and contains slowly conducting fibres responsible for “Second Pain” and has connections with brainstem, limbic and subcortical regions.

Thalamic terminus:

Most of the fibres of spinothalamic tract terminate in the nucleus ventro posterolateralis which is the major sensory relay nucleus. The other fibres terminate in the posterior group of nuclei, ventrobasal complex and hypothalamic nuclei.

THIRD ORDER NEURONS / THALAMOCORTICAL PROJECTIONS:

Posterior thalamic nuclei project to the post central cortex and upper bank of sylvian fissure and subserve tactile and proprioceptive stimuli with discriminative sensory function. Pain afferents received from mesencephalic offset of anterolateral funiculus project to the amygdaloid nuclei and other areas related to affect the emotion.

PERCEPTION OF PAIN :

The threshold for the perception of pain is the lowest intensity of stimulus recognized as pain. The conscious awareness or perception of pain occurs at the thalamic level and thalamic pain occurs when the thalamocortical pathway is destroyed. Somatosensory cortex is essential for the accurate localization, appreciation of intensity and other discriminative aspects of pain. Prefrontal cortex subserves the unpleasant affective and emotional reaction to pain.

GATE CONTROL THEORY OF PAIN:

It was propounded by Melzack and Walls in 1965. It states that modulation of pain impulses in the dorsal horn can control further synaptic transmission via the spinothalamic tract. It states that stimulation of large afferent fibres excite the I cells (inhibitory cells) in the lamina 2 and 3 of dorsal horn which in turn cause pre and post synaptic inhibition of secondary transmission neurons (T cells) in lamina 5 of dorsal horn and interrupt pain pathway. Conversely stimulation of small pain afferents (C fibres) inhibit the I cells leaving the T cells in the excitatory state thus facilitating transmission of pain.

Endogenous opioids and spinal modulation of pain perception:

Hughes et al described endogenous morphine like substances with analgesic activity called endorphins. There are 5 endorphins,

- Metenkephalin,

- Leuenkephalin,
- Betaendorphin,
- L endorphin
- R endorphin.

Metenkephalin and Leuenkephalin:

They are inhibitory neurotransmitters at the primary afferent nociceptive site. They act through release of substance P.

Dynorphins:

Control nociception at the spinal cord level through activation of kappa receptors. It is present in lamina 1 to 5 of dorsal horn.

L-endorphin and R- endorphins :

Breakdown products of beta endorphins.

4. PHARMACOLOGY OF OPIOIDS

Opium is extracted from the capsule of a poppy plants (Papaver somniferum). It is a brown residual material and has two active alkaloid ingredients, phenanthrene derivatives and benzoisoquinoline derivatives. Morphine, codeine and thebaine are derivatives of the former while papaverine and noscapine are derivatives of the latter compound. Morphine is naturally available at 10% concentration in wild poppy.

Classification of opioids:

Natural opioids: Morpine, Codeine

Semisythetic opioids: Diacetylemorphine and Pholcodine

Synthetic opioids: Pethidine, Fentanyl, Methdadone, Tramadol

LOCATION OF OPIOID RECEPTORS:

Opioid receptors are located in the areas of brain (periaqueductal gray matter of brainstem, amygdale, corpus striatum, hypothalamus) and spinal cord (substantia gelatinosa) that are involved in pain perception, integration of pain impulses and responses to pain.

Opioid receptors			
μ_1	μ_2	κ	δ
Analgesia	Analgesia(spinal)	Analgesia	Analgesia
Euphoria	Depression of ventilation	Dysphoria	Depression of ventilation
Miosis	Constipation	Miosis	Constipation

Table 4 shows actions of opioid receptor

	Mu (μ)	**Delta (δ)**	**Kappa (κ)**
Fentanyl	+++	+++	+++
Morphine	+++		+
Sufentanil	+++	+	+
Nalbuphine			++
Butarphanol			+++

Table 5. shows effects of opioids on receptor affinity

Drug	analgesia	Respiratory depression	Antitussive effect	constipation	Dependence liability
Mixed Opioid Agonist antagonist					
Pentazocine	+++	++	**0**	+	+
Butarphanol	+++	++	**0**	+	+
Nalbuphine	+++	++	**0**	+	+
Buprenorphine	+++	++	+	++	+

NALOXONE:

Pure opioid receptor antagonist. Recommended dose is 0.4 – 0.8 mg. When carefully titrated and administered it often restore spontaneous ventilation without reversal of adequate analgesia. Onset of action is 1 – 2 minutes with half life of 30 – 60 minutes.

NALTREXONE:

Pure opioid antagonist, long acting than naloxone. Duration of action is 30 – 90 minutes. Effective oral prophylactic against pruritus and vomiting associated with intrathecal morphine.

General Pharmacological Actions of opioids:

Analgesia:

Morpine is the most efficacious analgesic. The analgesia is dose dependent. Dull visceral pain is better relieved than sharp somatic pain. The degree of analgesia is dose dependent. At high doses it can relieve even very sharp somatic pain and to a very high degree. It is most effective at relieving nociceptive pain arising from stimulation of nerve endings compared to neuropathic pain.

Intrathecal injection has been shown to cause segmental analgesia without affecting other modalities of sensation, while in the spinal cord it acts directly on the substansia gelatinosa to inhibit release of excitatory neurotransmitters from the afferent fibres.

Sedation:

Indifference to self and surroundings accompanied by drowsiness occurs. This differs from hypnotics in that there is no motor incoordination involved. With increase in dose, sleep and coma can occur.

Respiratory center:

The respiratory center gets depressed and both rate and tidal volume are affected. Multiple instances of death due to overdose have been recorded. In addition to depression of the respiratory center, there is indifference to breathing

by the apneic patients themselves. They may not breath unless commanded to do so.

Mood and other subjective effects:

Opioids have a calming effect on the general population. There is loss of apprehension and a feeling of detachment. There is a lack of initiative and mental clouding. All of these are perceived as unpleasant sensations in the absence of pain. The feeling of detachment is described as “floating” by addicts.

Cough center:

The cough center is affected more than the respiratory center. Cough reflex is suppressed severely even at low doses. This is being used in cough suppressants like codeine.

Cardio-vascular system:

Morphine causes differential vasodilation which is greater in the systemic circuits compared to the pulmonary circuits resulting in a shift of blood to the systemic circulation. The vasodilation is mediated by multiple mechanisms including release of histamine, a direct depressant action on the vasomotor center and a direct action on the tone of the vessels. This results in overall reduced cardiac output due to the decreased peripheral resistance.

Neuroendocrine system:

Hypothalamic afferent collaterals are suppressed. There is universal suppression of all neuro-endocrine secretion. The posterior pituitary is affected more than the anterior pituitary. But these effects are short-lived and tolerance develops to these effects immediately.[7]

GIT:

Constipation is a major result of the action of morphine. There is increased tone and segmentation movements but decreased propulsive movements. Spasm of pyloric, ileocaecal and anal sphincters can occur. There is also central action causing inattention to defecation reflex.

Other smooth muscles:

Morphine causes spasm of the sphincter of Oddi. This can result in increased biliary pressure and biliary colic. The tone of both detrusor and the sphincter is increased resulting in difficulty in micturition and a feeling of urgency. It may slightly prolong labor and cause significant broncho constriction in asthmatics due to the release of histamine.

Pharmacokinetics:

A high and variable first-pass metabolism results in poor oral absorption of morphine with only about 20-25% bioavailability. There is a very high amount of distribution in the tissues compared to the plasma resulting in a high volume

of distribution. The half-life of the drug ranges from 4-6 hours because of the extensive tissue distribution.

Adverse Effects:

Dysphoric effects like sedation, lethargy and clouding of cognition can occur. Vomiting, constipation and respiratory depression are common even at low therapeutic doses. Blurring of vision and urinary retention can occur in the elderly. Hypotension can occur in mobile patients. Allergic reactions have been reported but are few and far between. Local reactions at the sites of injections are more common .

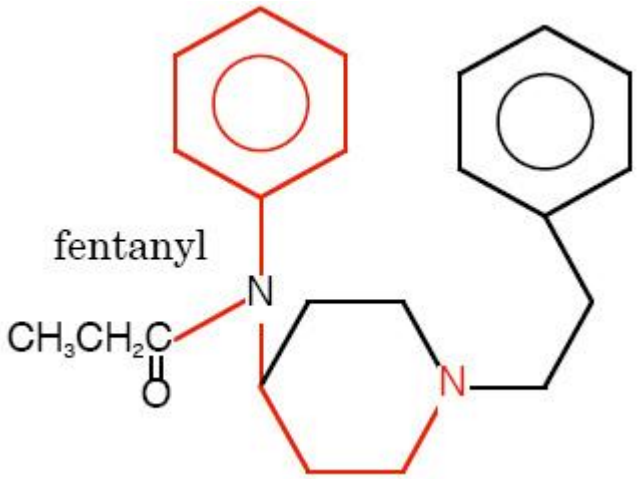
Dependence and Tolerance:

Morphine exhibits a high degree of tolerance.Tolerance occurs for all actions except constipation and miosis.Subjects tolerant to morphine exhibit tolerance to most CNS depressants as well. Withdrawal leads to drug seeking behavior in patients. Physical manifestations seen are mostly the opposite of the effects – lacrimation, sweating, diarrhea, mydriasis, hyperventilation, vasoconstriction and if prolonged weight loss and suicidal tendencies.

Interactions:

Tricyclic anti-depressants, Mono-amine oxidase, phenothiazine, amphetamines and neostigmine potentiate the effect of morphine. Morphine in turn retards the digestion of drugs by delaying gastic emptying.

PHARMACOLOGY OF FENTANYL



Structural formula of fentanyl

Synthetic opioid related to the phenylpiperidines. The actions of fentanyl is similar to those of μ-receptor agonists.

PHARMACOLOGICAL PROPERTIES

100 times more potent than morphine, most commonly administered intravenously, can be administered through epidural, intrathecal, transdermal and, oral route. The plasma concentration of fentanyl required for postoperative analgesia was approximately 1.5 ng / ml[8]

The advantage of liphophiicity is that the risk of delayed respiratory depression is less when compared with morphine . The time to peak analgesic effect after intravenous administration is 5 minutes. Fentanyl has high degree of cardiac stability due to less effect on heart rate and blood pressure, minimal myocardial depression with no release of histamine. High doses of fentanyl or

sufentanil are commonly used as the primary anesthetic for patients undergoing cardiovascular surgery.

Fentanyl	**Dose**
As Analgesic	**2 – 6 µg / kg**
As infusion	**0.5 – 5 µg / kg / hr**
For induction	**4 – 20 µg / kg**

Table 7 showing various dosage of fentanyl

PHYSIOCHEMICAL PROFILE:

Molecular weight	528.29
pKa	8.4
% unionized at pH 7.4	8.5%
% bound to plasma proteins	84%
Potency	100 > than morphine

Table 8 showing physiochemical properties of fentanyl

PHARMACOKINETIC PROFILE:

Volume of distribution at steady state	335 litres
Clearance	1530 ml / minutes
Effect site equilibration time	6.8 minutes
Hepatic extraction ratio	0.8 – 0.1
Context sensitive half time	260 minutes
Elimination half time	3.1 – 6.6 hours
First pass pulmonary uptake	75%

Table 9 showing pharmacokinetics of fentanyl

PHARMACOLOGY OF STEROIDS

Two classes of steroids:

The corticosteroids, and androgens.

The corticosteroids are classified as glucocorticoid (carbohydrate metabolism–regulating) and mineralocorticoid (electrolyte balance–regulating). The important glucocorticoid and mineralocorticoid in human is cortisol and aldosterone respectively.

GENERAL MECHANISMS FOR CORTICOSTEROID EFFECTS:

Interaction with specific receptor proteins in target tissues upregulate the expression of corticosteroid-responsive genes, which changes the levels and array of proteins synthesized by the various target tissues.

MOLECULAR MECHANISM OF ANTI INFLAMMATORY EFFECTS OF GLUCOCORTICOIDS:

Glucocorticosteroids are potent anti-inflammatory agents. This anti-inflammatory effect may be produced via a variety of mechanisms. A group of structurally related, calcium-dependent phospholipid-binding proteins, annexins, which were formerly known as lipocortins or calpactins, had been shown to be inducible by glucocorticoids. Annexin I has been reported to inhibit $sPLA_2$ activity in vitro. These observations led to the hypothesis that the

inhibition of $sPLA_2$ by annexins is the mechanism of the anti-inflammatory action of glucocorticoids.[9]

The prolongation of analgesic duration of perineural administration of dexamethasone may be secondary to local action on nociceptive- C fibres mediated via glucocorticoid receptors and upregulation of function of potassium channels in excitable cells

CARBOHYDRATE AND PROTEIN METABOLISM :

Stimulation of glucose synthesis from amino acids and glycerol and storage as glycogen in liver. There is diminished glucose utilisation with increased protein breakdown in the periphery resulting in increased blood glucose. Glycemic control can be worsen in patients taking corticosteroids.

LIPID METABOLISM:

Redistribution of body fat results in increased fat accumulation in supraclavicular area, nape of the neck, face along with a loss of fat in the extremities. An increase in free fatty acid level occurs due to augmentation of lipolytic effects of growth hormone and adrenergic agonists.

ELECTROLYTE AND WATER BALANCE :

In patients with glucocorticoid deficiency there is increased secretion of vasopressin, which stimulates water reabsorption in the kidney. Steroids interfere with Ca^{2+} uptake in the gut and increase Ca^{2+} excretion by the kidney leading to decreased total body Ca^{2+} stores. The most striking cardiovascular effects of corticosteroids result from mineralocorticoid-induced changes in renal

Na+ excretion, leading to increased sodium and water retention in primary aldosteronism there is enhanced response to vasoactive drugs.

SKELETAL MUSCLE:

In Addison's disease, weakness , fatigue and diminished work capacity are the prominent symptoms. In primary aldosteronism weakness and fatigue occurs due to steroid myopathy.

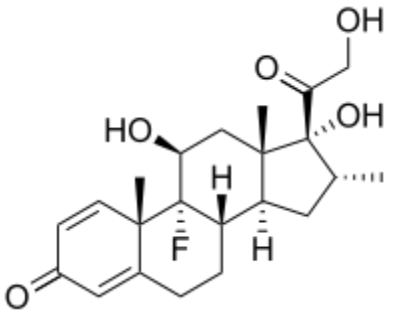
CENTRAL NERVOUS SYSTEM:

Patients with adrenal insufficiency exhibit apathy, depression and irritability. Replacement therapy will alleviate such symptoms. Treatment with glucocorticoids may result in behavioural changes such as mania, insomnia and restlessness and these abnormalities disappear with cessation of therapy.

BLOOD AND FORMED ELEMENTS:

Corticosteroids exert minimal effects on erythrocytes and haemoglobin as evident by polycythemia in cushing syndrome, an normocytic normochromic anaemia in addisons disease. A single dose of hydrocortisone can decrease the circulating levels of these cells within 4-6 hours . This persists for 24 hours and it results from redistribution of cells away from periphery.

PHARMACOLOGY OF DEXAMETHASONE:



Structural formula of dexamethasone

PHARMCOKINETICS OF DEXAMETHASONE

Bioavailability	80 – 90 %
Protein binding	70 %
Metabolism	hepatic
Half life	36 – 54 hours
Excretion	renal
Molecular weight	392.4 g / mol

Table 10 showing pharmacokinetics of dexamethasone

Dexamethasone is a high potency, long acting glucocorticoid with little mineralocorticoid effect. It has been used intravenously for prophylaxis of postoperative nausea. Single doses of epidural dexamethasone and other glucocorticoids have been reported to improve analgesia after various surgeries.

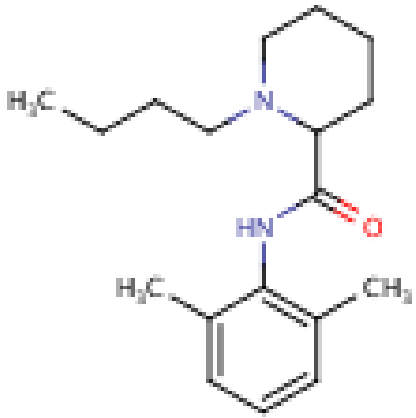
Acute noxious stimulation of peripheral tissues leads to sensitization of dorsal horn neurons of the spinal cord by the release of excitatory amino acids

such as glutamate and aspartate. These amino acids activate N-methyl-D-aspartate receptors resulting in calcium ion influx. As a result, increased intracellular calcium activates phospholipase A_2 which converts membrane phospholipids to arachidonic acid. Simultaneously, there is up-regulation of the expression of cyclo-oxygenase 2 in the spinal cord, leading to prostaglandin E_2 synthesis, which results in a hyperalgesia.

MECHANISM OF ACTION OF EPIDURAL STEROIDS:

Dexamethasone and other steroids act by suppression of transmission in thin unmyelinated C fibres while not affecting myelinated A_β fibres. It exerts these action through direct membrane stabilising effect and indirectly through mediators.These direct and indirect actions lead to decrease in intraneuronal edema and venous congestion thereby reducing ischemia and improving pain.

5. PHARMACOLOGY OF BUPIVACAINE



Structural formula of bupivacaine

It is an amide local anaesthetic first synthesized in Sweden by Ekenstam and his colleagues in 1957 and used clinically L.J.Telivuo in 1963. Its molecular weight is 288. (1-butyl- N-(2,6, dimethyl phenyl piperidine-2-carboxamide)

Prepared as a clear solution of 0.25%, 0.5% solution of bupivacaine hydrochloride. The hyperbaric solution used for subarachnoid block contains 80 mg / ml of glucose.

PHARMACOKINETICS:

At pH 7.4 only 15% exist in non ionised form. Absorption depends on the site of injection, dosage and use of epinephrine.

pKa	8.1
Protein binding	95 %
Lipid solubility	28 %

Volume of distribution	73 litre
Clearance of drug from plasma	0.471 litre / minute
Elimination half life	210 minute
Onset time	5 – 7 minute

Table 11 showing pharmacokinetics of bupivacaine

MECHANISM OF ACTION:

Local anesthetics such as bupivacaine block the generation and conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the prolongation of the nerve impulse and reducing the rate of rise of the action potential. The progression of anesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibres. The analgesic effects are thought to be due to its binding to the prostaglandin E2 receptors.

METABOLISM:

The possible pathway for metabolism of bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Only the N-dealkylated metabolite N-desbutyl bupivacaine has been measured in the blood or urine.5 % of the dose is excreted in the urine as pipcolloxylidine.16 % is excreted unchanged.

ROUTES OF ADMINISTRATION:

May be administered by infiltration, intrathecally or epidurally and for peripheral nerve blocks. The total dose of bupivacaine should not exceed 2 – 3 mg / kg (with or without epinephrine).

SYSTEMIC TOXICITY:

CARDIOVASCULAR SYSTEM:

Bupivacaine is markedly cardiotoxic. It binds to specific myocardial proteins. In toxic concentrations the drug decreases the peripheral vascular resistance and myocardial contractility producing hypotension and cardiovascular collapse. Cardiotoxic plasma concentration is 8 – 10 µg / ml.

20 % intra lipid can be given for bupivacaine toxicity. The dose is 1.5 ml / kg as initial bolus can be repeated 1 to 2 times for persistent asystole. Infusion can be started at dose of 0.25 ml / kg / min for 30 – 60 min.

CENTRAL NERVOUS SYSTEM:

During accidental overdosage or direct vascular injections the clinical signs are numbness of tongue, light headedness, visual and auditory disturbances, muscle twitching, tremors. The signs may progress to generalised convulsions of the tonic clonic nature. The typical plasma concentrations of bupivacainne associated with seizures is 4.5 – 5.5 µg / ml.

6. METHODS OF POST OPERATIVE ANALGESIA

SYSTEMIC OPIOIDS:

Parenteral opioid analgesics are one of the cornerstone options for the treatment of postoperative pain. These agents generally exert their analgesic effects through μ-receptors in the CNS. Opioids may be administered by the subcutaneous, transdermal, transmucosal, or intramuscular route, but the most common routes of postoperative systemic opioid analgesic administration are oral and intravenous. Opioids may also be administered at specific anatomic sites such as the intrathecal or epidural space .

INTRAVENOUS PATIENT CONTROLLED ANALGESIA:

Intravenous patient-controlled analgesia (PCA) optimizes delivery of analgesic opioids and minimizes the effects of pharmacokinetic and pharmacodynamic variability in individual patients. Although some equipment related malfunctions have been reported, the PCA device itself is relatively free of problems. Most of the problems related to PCA use result from user or operator error.

The lockout interval may also affect the analgesic efficacy of intravenous PCA. In essence, the lockout interval is a safety feature of intravenous PCA, and most intervals range from 5 to 10 minutes.

NON STEROIDAL ANTI INFLAMMATORY AGENTS:

NSAIDs generally provide effective analgesia for mild to moderate pain. NSAIDs are also traditionally considered a useful adjunct to opioids for the treatment of moderate to severe pain. NSAIDs may be administered orally or parenterally, rectally and are particularly useful as components of a multimodal analgesic regimen by producing analgesia through a different mechanism from that of opioids or local anesthetics. Few NSAIDS that are commonly used includes Diclofenac (50 – 75 mg IM), Ketorolac (30 mg IM), paracetamol IV 15 – 20 mg / kg.

KETAMINE HYDROCHLORIDE:

Perioperative subanesthetic doses of ketamine reduce rescue analgesic requirements or pain intensity. It reduces 24-hour PCA morphine consumption and postoperative nausea or vomiting and had minimal adverse effects. Ketamine has also been administered epidurally and intrathecally, but racemic mixtures of ketamine have been found to be neurotoxic and therefore the use of neuraxial ketamine is discouraged.

REGIONAL ANALGESIA TECHNIQUES:

The analgesia provided by epidural and peripheral techniques is superior to that with systemic opioids and use of these techniques may even reduce morbidity and mortality. It includes

- Local anesthetic infiltration
- Nerve blocks
- Peripheral or plexus block
- Epidural – single shot, continous infusion, patient controlled epidural anesthesia
- Intrathecal – single shot, continous infusion.

DOSING OF COMMON NEURAXIAL OPIOIDS:

DRUG	Intrathecal single dose	Epidural single dose	Epidural infusion
Fentanyl	5-25 µg	50-100 µg	25-100 µg/hr
Sufentanil	2-10 µg	10-50 µg	10-20 µg/hr
Morphine	0.1-0.3 mg	1-5 mg	0.1-1 mg/hr
Pethidine	10-30 mg	20-60 mg	10-60 mg/hr

Table 12 showing dosage of common neuraxial opioid

Administration of a single dose of opioid may be efficacious as a sole or adjuvant analgesic agent when administered intrathecally or epidurally. The site of analgesic action for hydrophilic opioids is spinal. A single bolus of epidural fentanyl may be administered to provide rapid postoperative analgesia, however diluting the epidural dose of fentanyl (typically 50 to 100 µg) in at least 10 mL of normal saline is suggested to decrease the onset and prolong the duration of

analgesia, possibly as a result of an increase in initial spread and diffusion of the lipophilic opioid[11] Single-dose epidural morphine is effective for postoperative analgesia and may decrease postoperative patient morbidity in selected patients but is associated with following adverse effects.

ADVERSE EFFECTS:

- Hypotension
- Nausea and vomiting
- Pruritus
- Respiratory depression
- Urinary retention
- Mental state changes
- Central nervous system excitation
- Herpes labialis reactivation
- Gastrointestinal dysfunction.

CONTINUOUS EPIDURAL ANESTHESIA & ANALGESIA:

Analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of acute postoperative pain. Postoperative epidural analgesia can provide analgesia superior to that with systemic opioids Insertion of the epidural catheter congruent to the incisional dermatome results in optimal postoperative epidural analgesia by infusing analgesic agents to the

appropriate incisional dermatomes, providing superior analgesia, minimizing side effects (e.g., lower extremity motor block and urinary retention), and decreasing morbidity. Combination of opioid with local anaesthetic ,opioid,or local anaesthetic alone can be used for infusion.

PATIENT CONTROLLED EPIDURAL ANALGESIA (PCEA)

. PCEA allows individualization of postoperative analgesic requirements and may have several advantages over continous epidural infusion, including lower drug use and greater patient satisfaction

Analgesic solution	Continous rate ml/hr	Demand dose ml	Lockout interval ml/min
0.05%Bupivacaine+4µg/ml Fentanyl	4	2	10
0.0625%Bupivacaine+5µg/ml Fentanyl	4-6	3-4	10-15
0.1%Bupivacaine+5µg/ml Fentanyl	6	2	10-15
0.2%Ropivacaine+5µg/ml Fentanyl	5	2	20

Table 13 Patient controlled epidural analgesia regimens.

THORACIC PARAVERTEBRAL BLOCK:

Used for thoracic, breast, upper abdominal surgery and for the treatment of rib fracture pain.probable site of action include somatic and sympathetic nerve with epidural blockade. Can be administered as single injection or as continous infusion.

INTERPLEURAL ANALGESIA:

Inferior to epidural and paravertebral analgesia for control of postoperative pain, preservation of lung function after thoracotomy.

INTRA ARTICULAR ANALGESIA:

Local peripheral administration of opioids (e.g intra-articular injection after knee surgery) may provide analgesia for up to 24 hours after surgery and decrease the incidence of chronic pain. Peripheral opioid receptors are found on the peripheral terminals of primary afferent nerves and are upregulated during inflammation of peripheral tissues.

OTHER TECHNIQUES:

TENS(transcutaneous electrical nerve stimulation), acupuncture and psychological approaches.

7. REVIEW OF LITERATURE

1. Youn yi jo et al[13] compared outcomes of epidural ropivacaine 0.25% and epidural ropivacaine 0.25% with dexamethasone 5 mg in patients undergoing radical subtotal gastrectomy.He compared VAS scores and rescue analgesic requirements among these group of patients and concluded that VAS scores and rescue analgesic requirements were less in dexamethasone treated group.
2. Farshad M Ahadian et al[14] in his study compared the efficacy of three different doses(4 mg, 8 mg, 12mg) of transforaminal epidural dexamethasone in relieving radicular pain.He measured the outcomes in terms of VAS scores and subject satisfaction scale.It showed that improvement in radicular pain with no difference in efficacy of different doses of dexamethasone.
3. Wang et al[15] compared the effect of epidural dexamethasone in relieving post epidural backache in patients undergoing hemorrhoidectomy. In the study group I patients received 25 cc of 2% lignocaine with 1 cc normal saline. Group II patients received 25 cc of 2% lignocaine with 5 mg dexamethasone. He found decreased severity of backache in group II patients.
4. Thomas et al [16] evaluated the efficacy of epidural dexamethasone in reducing post operative analgesic requirements following laprascopic

cholecystetcomy. In that study group I patients received IV dexamethasone 5 mg and 8 cc of 0.25% bupivacaine epidurally. Group II patients received IV normal saline 2 cc with 8 cc of 0.25% bupivacaine and dexamethasone epidurally. He concluded in the study that group II patients receiving epidural dexamethasone 5 mg had effective post operative pain relief and less systemic opioid requirements following laprascopic cholecystectomy.

5. Jehan et al [17] studied the effect of preoperative epidural dexamethasone and magnesium sulphate in patients undergoing abdominal surgeries. In the study, group I patients received 12cc of 0.5% bupivacaine with morphine 2 mg and magnesium sulphate 50mg epidurally. Group II patients received 12 cc of 0.5%bupivacaine with morphine 2 mg and dexamethasone 6 mg epidurally. He concluded that with co administration of magnesium sulphate 50 mg or dexamethasone 6 mg as a single dose in preoperative period was associated with less postoperative narcotic consumption and VAS scores.
6. W.Neill et al [18] studied the effects of epidural methyl prednisolone 40 mg and morphine 5mg along with control group having normal saline in patients undergoing surgery for spinal stenosis. He found that the postoperative analgesic requirement was less in group of patients receiving epidural morphine or methylprednisolone or combination of both.

7. Atsuhiro Kikuchi et al[19] studied the effect of intrathecal and epidural methyl prednisolone in relieving the severity of pain due to post herpetic neuralgia. Group I patients received 40 mg of methylprednisolone epidurally and group II patients received 40 mg of methylprednisolone intrathecally. He concluded that pain severity was less in patients receiving intrathecal methylprednisolone due to decreased inflammatory reaction in CSF.
8. Saeid Abrishamkar et al[20] studied the effect of epidural methylprednisolone 40 mg and local anesthetic (1 cc of 0.5% bupivacaine) impregnated in adipose tissue in relieving low back pain and radicular pain in lumbar disc surgery. He found that combination of methylprednisolone and local anaesthetic increased the duration of pain free interval.
9. Park CH[21] compared the effects of transforaminal injection of dexamethasone 7.5 mg and triamcinolone 40 mg in patients with lumbar disc herniation and found that triamcinolone is more effective in relieving lumbar radiculopathy than dexamethasone.
10. Hudan et al[22] compared the pain relief in patients with lumbar canal stenosis by epidural administration of methylprednisolone 80 mg along with 0.125% bupivacaine and triamcinolone 80 mg with 0.125% bupivacaine epidurally. He found better pain relief in patients receiving epidural methylprednisolone.

11. Khafagy et al[23] studied the effect of epidural dexamethasone in patients undergoing lower abdominal surgeries. In that study group I patients received epidural 10cc of 0.25% bupivacaine and fentanyl 50µg epidurally and group II patients received 10cc of 0.25 bupivacaine with dexamethasone 4 mg. He found that addition of epidural dexamethasone improved postoperative pain relief and decreased analgesic requirement.
12. Guilfoyle MR[24] studied the effect of epidural fentanyl in patients undergoing surgery for lumbar canal stenosis. In the study group I patients received normal saline epidurally at the end of surgery and group II patients received epidural fentanyl 100 µg . Postoperative pain relief was compared with VAS scores which showed effective post operative analgesia in group of patients receiving bolus epidural fentanyl.
13. Ganesh A et al[25] studied the effects of epidural fentanyl infusion for post operative analgesia in infants undergoing thoracotomy . One group of patients received epidural infusion of 0.1 % bupivacaine and other group received epidural infusion of 0.1% bupivacaine with fentanyl 2µg / ml . He concluded that there was improved analgesia in group receiving fentanyl infusion with better pain scores and less rescue analgesic requirements with nalbuphine.
14. Szabova A et al[26] - postoperative epidural butorphanol / bupivacaine with the epidural analgesic infusion fentanyl / bupivacaine in children. Epidural fentanyl provided similar analgesia to epidural butarphanol

after urological procedures in children, but butorphanol caused less pruritus than fentanyl. Epidural analgesia with butorphanol / bupivacaine is effective than epidural fentanyl / bupivacaine in children undergoing urological procedures.

15. Marcelo Soares Privado[27] compared the effect of epidural versus intravenous fentanyl in patients undergoing orthopaedic procedure. Group I patients received 100µg fentanyl epidurally and group II patients received 100µg fentanyl intravenously. The study outcome was less need of supplementary analgesia with tenoxicam in group I patients receiving epidural fentanyl.

8. AIM OF THE STUDY

To compare the efficacy of epidural dexamethasone versus fentanyl on post operative analgesia

9. MATERIALS AND METHOD

After getting Ethical committee approval from Goverment Kilpauk Medical College Hospital. Chennai 10, we conducted the study in our hospital in 60 adult male patients aged between 25 – 45 years belonging to ASA Physical status I and II undergoing elective hernioplasty under epidural anesthesia after obtaining written informed consent.

STUDY DESIGN:

Double blinded randomized prospective study.

Patients were randomly allocated into one of the three groups (20 patients per group) by lotting method.

METHOD OF BLINDING:

Patients and the person performing the epidural technique was unaware of the epidural drug composition. The drug solution was prepared by an anaesthesiologist assistant in the operating room and was labelled accordingly.

PATIENT SELECTION:

All the 60 patients were evaluated clinically, biochemically and assessed for hernioplasty under epidural anesthesia considering the inclusion and

exclusion criteria. Then the patients were randomised into three groups.

STUDY PERIOD:

From onset of epidural blockade to onset of postoperative pain with VAS > 5.

OBSERVATION PERIOD:

For 24 hours postoperatively.

INCLUSION CRITERIA:

- Adult male patients aged 25 – 45 years
- ASA physical status I & II
- For uncomplicated inguinal hernia surgery

EXCLUSION CRITERIA :

- Patient unwilling for the procedure
- Obese
- Hypertension
- Diabetes mellitus
- History of peptic ulcer disease
- Those received corticosteroids or immune suppressive drugs in the last 6 months
- Those with contraindications to steroids
- Patients on anticoagulants

- Patchy or inadequate blockade which required supplemental narcotics or general anesthesia.

PATIENT GROUPS:

60 patients enrolled in the study were randomly allocated into three groups.

- Group 1: Patients receiving 11 cc of 0.5 % bupivacaine plus normal saline 1 cc epidurally.
- Group 2: Patients receiving 11 cc of 0.5 % bupivacaine plus 50 µg fentanyl epidurally.
- Group 3: Patients receiving 11 cc of 0.5 % bupivacaine plus 4 mg preservative free dexamethasone epidurally.

All patients received a total volume of 15 ml of study drug including 3 ml of test dose plus 1 ml of adjuvant. The level of blockade was then noted.

MATERIALS USED:

- 16 Gauge Tuohy needle
- 18 Gauge epidural catheter
- Loss of resistance syringe
- 10 ml syringe
- Local anesthetic solution (3 ml of 0.5 % bupivacaine with epinephrine 1 in 2,00,000 dilution) for test dose.
- 0.5% bupivacaine

- Inj. Fentanyl
- Inj. Dexamethasone sodium phosphate (preservative free)
- 22 g needle for pin prick test

PARAMETERS TO BE OBSERVED:

1.Demographic parameters

2. baseline parameters

3. onset of anesthesia

4.Time for two segment regression of sensory and motor blockade.

5. Duration of analgesia

6.Incidence of side effects like nausea, vomiting, sedation, hypotension

CONDUCT OF STUDY:

In the pre anesthetic visit, study plan was explained in detail to all the patients. Written informed consent obtained after explaining the study in their own langage.

After getting informed consent, patient was prepared for the surgery with fasting period of 8 hours. Antacid prophylaxis was given with inj. Ranitidine 50 mg IV 2 hours before surgery. Baseline vital parameters were recorded in the patient waiting room.

CONDUCT OF EPIDURAL BLOCK:

In the operating room patient was connected to five lead ECG, Non Invasive Blood Pressure, Pulse Oximeter and baseline parameters were recorded. An intravenous line was established with 18 gauge venflon and preloaded with 15 ml / kg of ringer lactate.

Under strict aseptic precautions with the patient in right lateral position local anaesthtic infiltration was given with 1 % lignocaine. Epidural space was identified at L2 – L3 space through 16 gauge Tuohy needle by loss of resistance technique. An 18 gauge epidural catheter was inserted in L2 – L3 space and 5 cm of catheter kept inside epidural space. Test dose was given with 3 ml of 0.5 % bupivacaine with epinephrine 1:2,00,000 dilution via catheter before it is fixed to rule out intravascular or intrathecal placement.

After confirming the epidural placement of the catheter, 12 ml of blinded study solution was given and level of blockade was noted at 5 min interval till 20 minutes. Oxygen at 4L/min via venturi mask was provided. If there was any hypotension (systolic blood pressure < 80 mm hg or mean arterial pressure < 60 mm hg) Inj. Ephedrine 6mg IV was given along with intravenous fluid. If the heart rate fell below 50 / minute, Inj. Atropine 0.6 mg IV was given. The respiratory rate and type of respiration was also monitored.

After the administration of study medication, the onset of analgesia and the level achieved was noted at 5 min interval. Surgery was allowed to proceed when the level of blockade was T8. Throughout the intraoperative period vitals like heart rate, systolic blood pressure, mean arterial pressure, oxygen saturation and respiratory rate were monitored.

CONCLUSION OF SURGERY:

At the end of surgery the level of sensory blockade was assessed and then epidural catheter was removed. The patient was shifted to recovery room and observed for 2 hour and vitals were recorded and shifted to Post Anesthesia Care Unit .

ASSESSMENT OF PAIN SCORE:

In the PACU, pain score was observed at 30 min, 60 min, 90 min, 180 min, & then every ½ hourly intervals upto 10hrs on a 10cm Visual analogue scale (‘no pain’ at 0 cm end and ‘worst pain ever’ at 10cm end) and for occurrence of side effects like nausea, vomiting, pruritus, respiratory depression, sedation and changes in hemodynamic variables.

ONSET AND DURATION OF ANALGESIA:

The time since injection of drug into epidural space to the time required to obtain sensory blockade upto T8 (loss of pin prick to 22 gauge needle) was

noted as onset of analgesia. The time between the onset of analgesia and return to baseline VAS of 5 was noted as the duration of analgesia .

RESCUE ANALGESIA IN THE POSTOPERATIVE PERIOD:

When the VAS score was more than 5 or when the patients complained of pain, Since the study was concluded Inj. Diclofenac 50mg was given intramuscularly and epidural catheter was removed.

The patients were followed for a period of 24 hours in PACU for any occurrence of nausea, vomiting, sedation, pruritus, respiratory depression (RR<10/min), and parameters like duration of analgesia, hemodynamic variables etc were noted.

Statistical analysis was done on collected data. Analysis of variances (ANOVA) was used for comparison of mean values between more than two groups. Posthoc test was used to find any significance between the individual groups.

VISUAL ANALOGUE SCALE:

" Please make a mark on this line that describes how much pain you are having"

No 0___1___2___3___4___5___6___7___8___9___10 Worst

pain pain

0- No nausea/vomiting

1- Nausea

2- Vomiting

0 - No pruritus

1 – pruritus

Bradycardia HR < 50 / min

0 – No bradycardia

1 – presence o bradycardia

Respiratory depression

RR < 10 / minute

0 – no respiratory depression

1 – presence of respiratory depression

Desaturation Spo2 < 95 %

0 – no desaturation

1 – presence of desaturation

Hypotension

Systolic blood pressure < 80 mm hg

Mean arterial pressure < 60 mm hg

VISUAL ANALOGUE SCALE

A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured (example -the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain).From the patient's perspective this spectrum appears continuous and their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised.Operationally a VAS is usually a horizontal line, 10cm / 100 mm in length. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in centimetres / millimetres from the left hand end of the line to the point that the patient marks.

10. OBSERVATIONS & RESULTS

As per the study methodology the data of 60 male patients aged 25 – 45 years belonging to ASA I & II undergoing elective hernioplasty were included in the study and were statistically analysed and compared .The demographic data was analysed and it was found to have statistically no significant difference in parameters such as age, height, weight, ASA status.

S.no	parameter	Group 1 (NS)	Group 2 (FENTANYL)	Group 3 (DEXA)	p value
1.	Age(yr)	31.10	31.95	32.65	0.908
2	Weight(kg)	61.33	60.05	62.74	0.707
3.	Height(cm)	159.28	160.50	159.72	0.985

Table 14 shows mean values of demographic parameters between groups

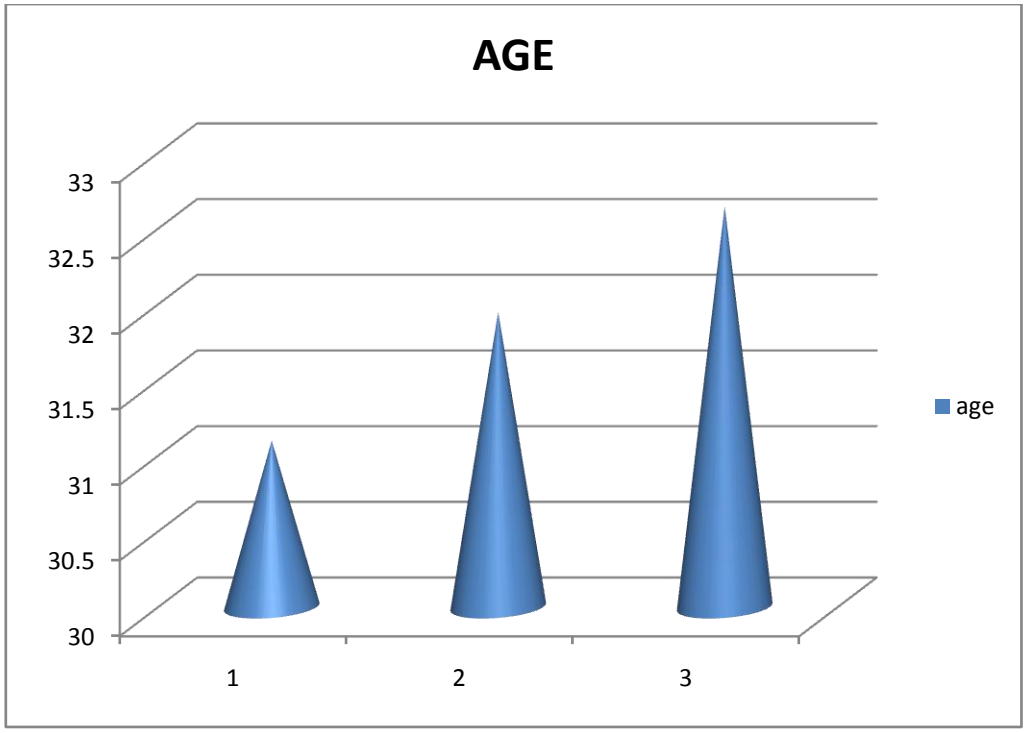


Chart – 1 Age distribution between three groups

The mean age of group1, group 2 and group 3 were 31.10, 31.95, 32.65 respectively. There was no statistically significant difference (p = 0.908) between the mean age of three groups, which shows these three groups were similar with respect to age.

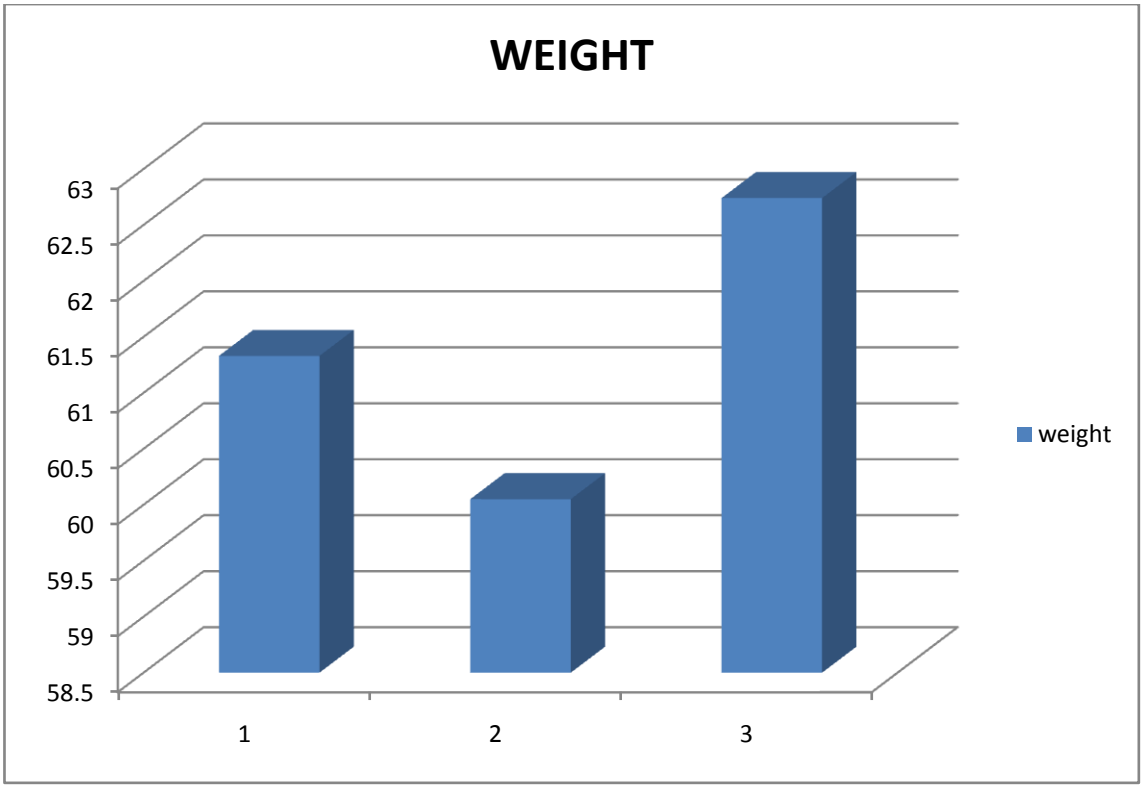


Chart – 2 Weight distribution (in kg) between three groups

The mean weight of group 1, group 2 and 3 were 61.33, 60.05, 62.74 respectively. There was no statistically significant difference (p = 0.707) between three groups, which shows these groups were similar with respect to weight.

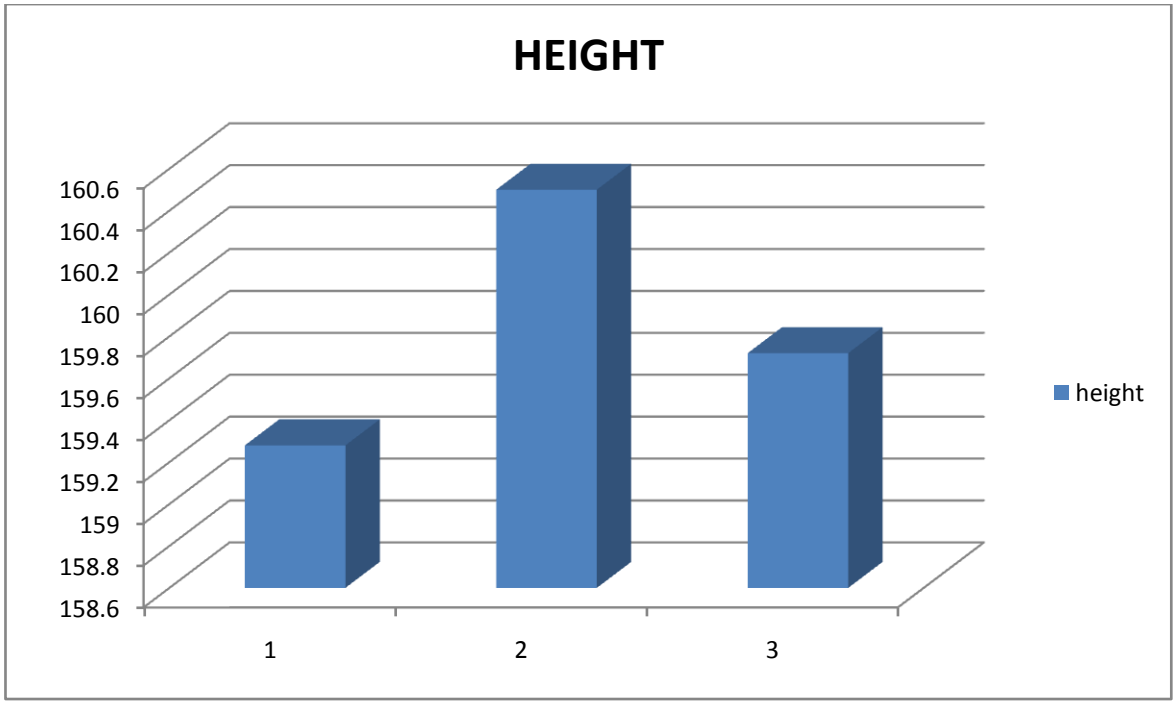


Chart – 3 Height distribution (in cm) between three groups

The mean height of group 1, 2, and group 3 were 159.28, 160.50, 159.72 respectively. There is no statistically significant difference between three groups which shows they are comparable with respect to height.

S.no	parameter	Group 1 (NS)min	Group 2 (FENT)min	Group 3 (DEXA)min	p value
1.	Onset of analgesia	5.300	5.075	6.525	0.003
2.	Duration	256.05	347.25	373.00	0.000

Table 15 showing onset and duration of analgesia between groups

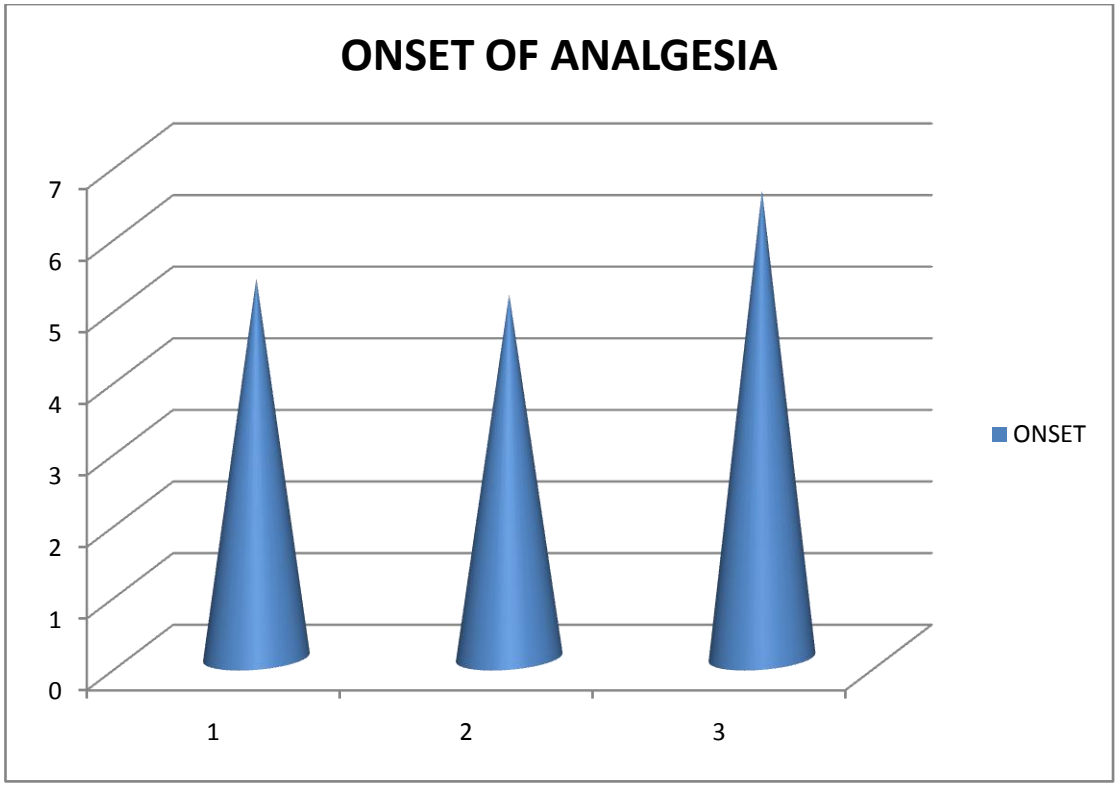


Chart – 4 diagram showing onset of analgesia significantly shorter in group 2 patients compared with group 1 and group 3.

On comparing the mean onset of analgesia between three groups, the group 2 patients receiving fentanyl (5.075 minutes) had shorter onset of time than group 1 patients receiving normal saline (5.300 minutes) and group 3 patients receiving dexamethasone (6.525 minutes).

The mean onset of analgesia among three groups

Group 2 < Group 1 < Group 3

Thus there was statistically significant difference in the mean onset of analgesia among the three groups. ($p < 0.05$).

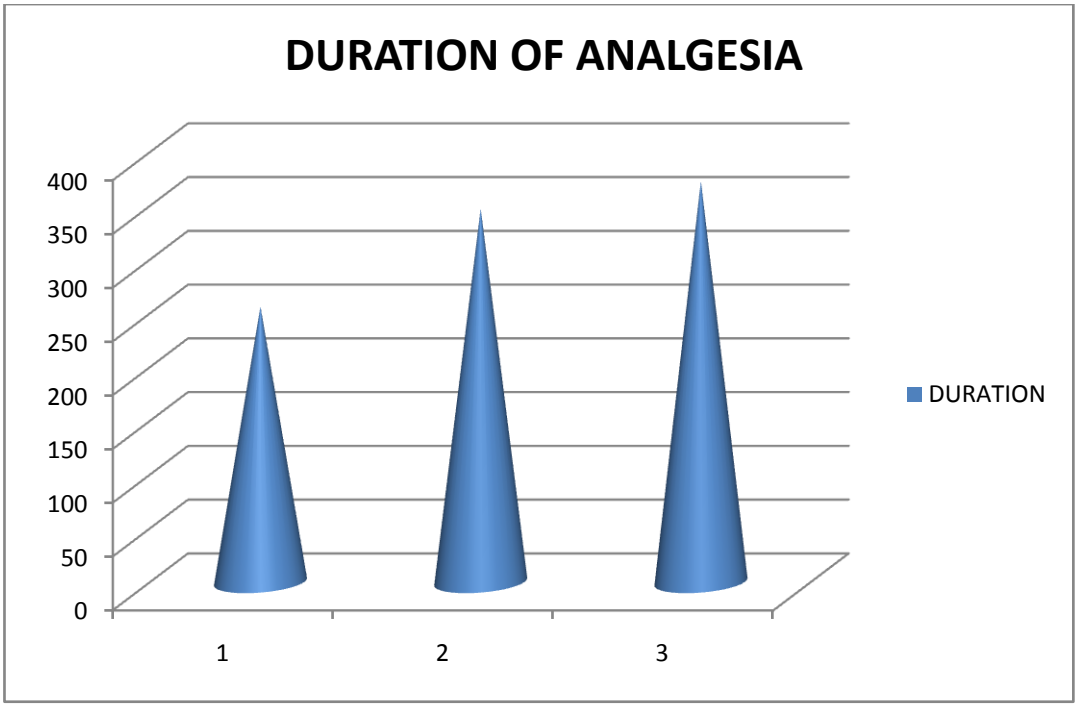


Chart – 5 Diagram shows duration of analgesia is significantly prolonged in group 3 patients compared with group 1 and group 2 patients.

On comparing the mean duration of analgesia among the three groups, group 3 patients receiving dexamethasone (373 minutes) had prolonged duration of analgesia than the group 2 (347.25 minutes) and group 1 patients (256.05 minutes).

Order of duration of analgesia

Group 3 > group 2 > group 1 Thus there was statistically significant difference in duration of analgesia between groups.

S.no	parameter	Group 1 (NS)	Group 2 (FENT)	Group 3 (DEXA)	p value
1.	Nausea	3.55%	20%	-	0.000
2.	pruritus	-	15%	-	0.033
3.	sedation	-	25%	-	0.000
4.	hypotension	10%	15%	20%	0.070

Table 16 shows side effects between three groups

The side effects like nausea, pruritus and sedation were noted in fentanyl receiving group than other groups. These side effects were statistically significant on comparing between groups. ($p < 0.05$). Hypotension was noted in all groups, but the incidence of hypotension is higher in group 3 patients receiving dexamethasone than group 2 patients receiving fentanyl and group 1 patients receiving normal saline. None of the patients had bradycardia or respiratory depression.

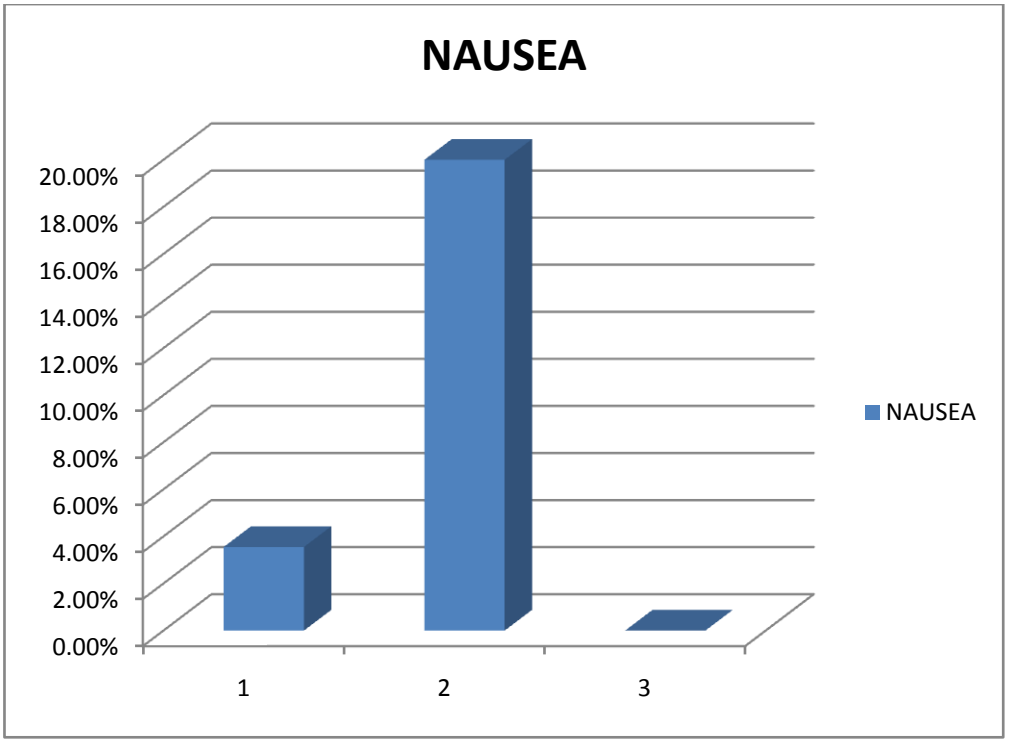


Chart – 6 diagram shows significantly higher incidence of nausea in group 2 patients.

The incidence of nausea in group 2 patients receiving fentanyl is 20 % and group 1 patients receiving normal saline is 3.5 %. There is nil incidence of nausea in group 3 patients receiving dexamethasone. This shows statistically significant incidence of nausea in fentanyl receiving group.

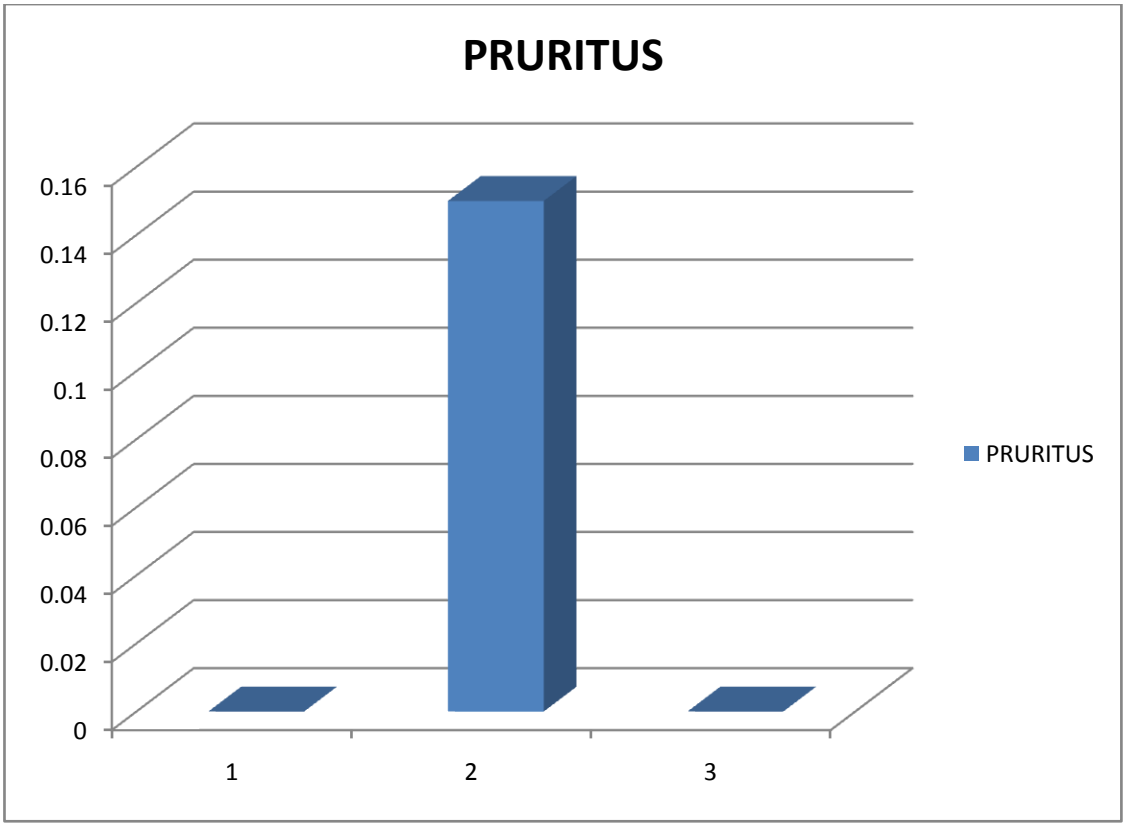


Chart – 7 diagram shows significantly higher incidence of pruritus in group 2

The incidence of pruritus in patients receiving fentanyl is 15 %. The incidence of pruritus is nil in patients receiving dexamethasone and normal saline. This shows statistically significant incidence of pruritus in fentanyl receiving group.

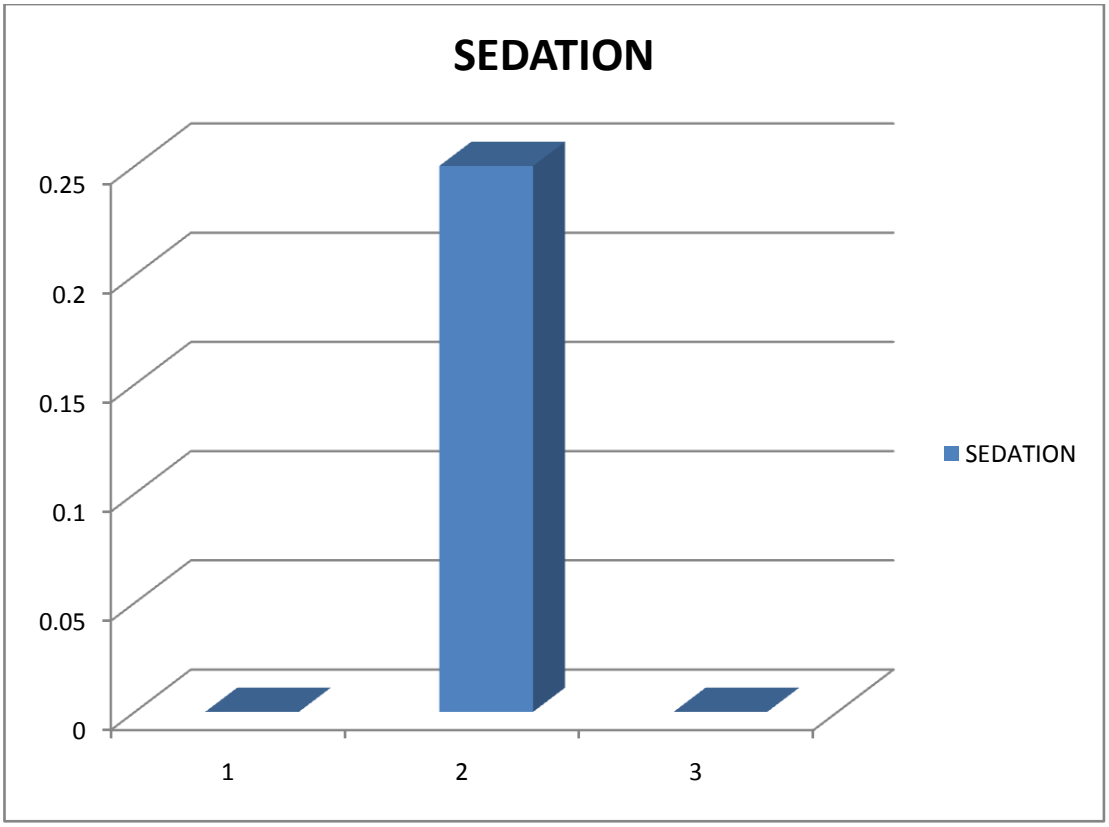


Chart – 8 diagram showing significantly higher incidence of sedation in group 2

The incidence of sedation was 25 % in group 2 patients receiving fentanyl. There was nil incidence of sedation in patients receiving dexamethasone and normal saline. This shows statistically significant incidence of sedation in patients receiving fentanyl .

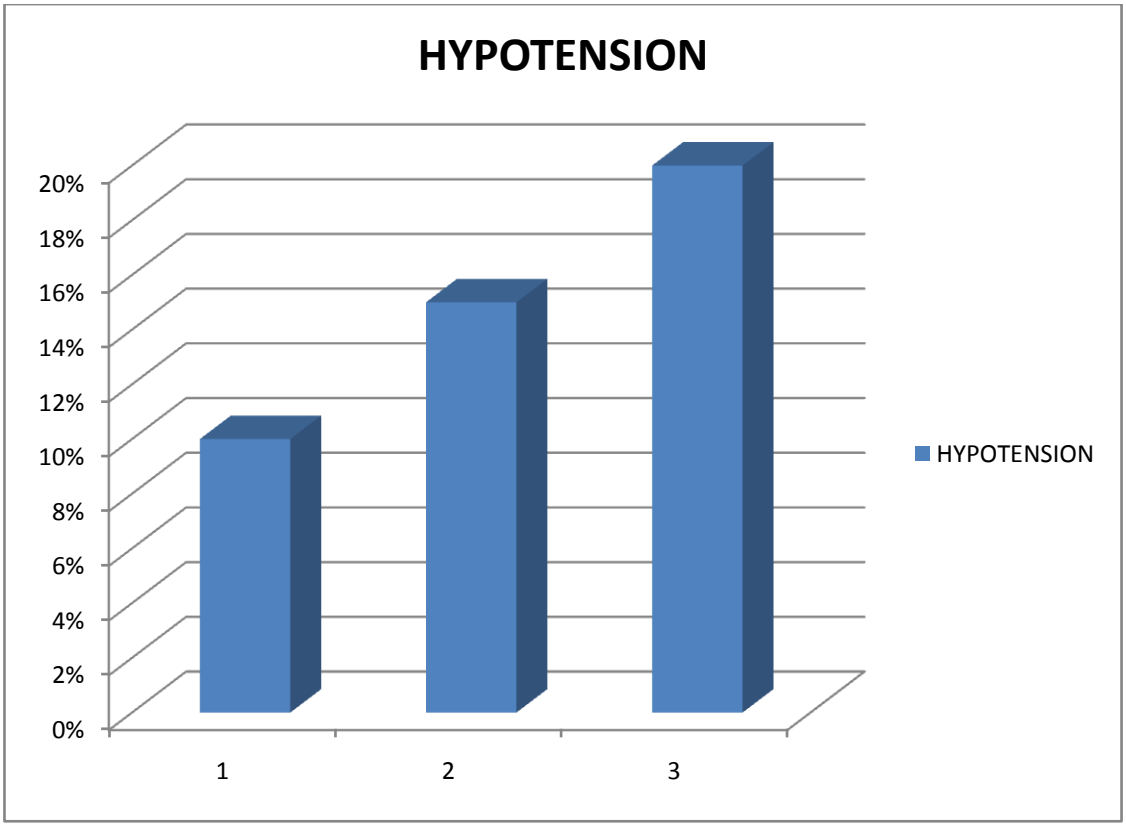


Chart – 9 diagram shows higher incidence of hypotension in group 3.

The incidence of hypotension in patients receiving dexamethasone, fentanyl, normal saline was 20 %, 15 %, 10 % respectively. This shows no statistically significant difference between three groups.

11. DISCUSSION

Based on the observations and results obtained in our study involving 20 patients in each group are discussed in detail by comparing with the available evidences in the literature. The analgesic efficacy of epidurally administered 0.5% bupivacaine + normal saline (group 1), 0.5% bupivacaine + 50 µg fentanyl (group 2) and 0.5% bupivacaine + 4 mg dexamethasone (group 3) was studied.

All the demographic variables like age, height, weight were comparable to each other. There is no statistically significant difference between the parameters. The two segment time regression was comparable between all the three groups.(table 14)

MEAN ONSET OF ANALGESIA :

In our study the mean onset of analgesia was earlier in group 2 patients receiving fentanyl (5.07 minutes) than group 1 patients receiving normal saline (5.30 minutes) and group 3 dexamethasone group (6.52 minutes). This was found to be statistically significant.($p < 0.05$) (table 15)

The onset of analgesia was earlier in the fentanyl group when compared to the control group. This study confirmed that onset of action is earlier with combination of opioid and local anaesthetic than local anesthetic alone. This finding correlates with the study done by **Manpreet Kaur et al**

who studied the effect of intrathecal bupivacaine alone and intrathecal bupivacaine along with opioids like butorphanol and sufentanil.

The onset of analgesia was earlier in the control group receiving normal saline (5.3 minutes) than compared compared with group 3 receiving dexamethasone (6.52 minutes). This correlates with study of **Youn Yi Joun et al** who concluded that epidural administration of dexamethasone 5 mg in patients undergoing radical subtotal gastrectomy resulted in less VAS scores and rescue analgesic requirements than control groups. The onset of action of epidural dexamethasone is still unclear.

MEAN DURATION OF ANALGESIA:

The duration of post operative analgesia was prolonged in group 3 patients receiving dexamethasone (mean 373 minutes) than in group 2 patients receiving fentanyl (347 minutes) followed by control group receiving normal saline(256 minutes).

The results of our study correlate with study done by **Khafagy et al**. In his study he concluded that epidural dexamethasone resulted in low post operative pain score and analgesic requirements and prolonged analgesic duration. Results of our study also correlate with the study of **Thomas & Beevi et al** who concluded that patients receiving epidural dexamethasone had less post operative VAS scores and analgesic consumption. Dexamethasone had

action at spinal cord level in addition to its action on the peripheral tissues after systemic absorption from epidural space.

TWO SEGMENT REGRESSION TIME:

The two segment regression time in group 1 and 2 was 120 min and 131.5 minutes respectively. The regression time was 122 min in group 3 patients. This was comparable with the three groups.

SIDE EFFECTS:

There was statistically significant difference in the incidence of nausea, sedation, and pruritus in group 3 patients receiving dexamethasone compared with group 2 patients receiving fentanyl and group 1 patients receiving normal saline. This correlated with the study done by **Bisgaard et al** who concluded that less incidence of nausea, pruritus, fatigue, overall pain following IV administration of dexamethasone 8 mg. There was no long term neurological complications in group 3 patients receiving dexamethasone.(table 16)

SUMMARY

After getting ethical committee approval the study was conducted in 60 patients undergoing elective hernioplasty belonging to ASA physical status I & II. The 60 patients enrolled in the study were divided into three groups.The data were statistically analysed , compared and discussed. The results obtained were summarised below:

1. The demographic data like age, weight, height were comparable to each other in all the three group.
2. The onset of analgesia was significantly earlier in group 2 patients receiving fentanyl 5.075 min and the onset was delayed in dexamethasone receiving group 6.525 min .
3. The duration of analgesia was significantly prolonged in group 3 patients receiving dexamethasone 373 min when compared to group 2 patients receiving fentanyl 347.25 min.
4. None of the patients in group 3 receiving dexamethasone had nausea. The incidence of nausea in group 1 was 3.55 % and in group 2 patients was 20%..
5. None of the patients in group 1 and group 3 had pruritus but the incidence of pruritus in group 2 patients receiving fentanyl was 15%.

6. There is nil incidence of sedation in group 1 and group 3.There was more incidence of sedation in group 2 patients receiving fentanyl (25 %.)
7. The incidence of initial hypotension followed by epidural bolus was 10, 15, 20 % in group 1, 2 and 3 respectively which were comparable. This initial hypotension was treated with fluid bolus and single dose of inj. Ephedrine 6 mg IV.
8. There is nil incidence of any complications in all the study group.

12. CONCLUSION

We conclude that epidural administration of dexamethasone – bupivacaine admixture resulted in better postoperative analgesia in terms of lower postoperative pain score, prolonged postoperative analgesia and patient comfort with fewer side effects when compared with the other two groups.

We also conclude that this epidural dexamethasone resulted in prolonged postoperative analgesia without any side effects like nausea, vomiting, pruritus, sedation except hypotension in few patients.

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ANNEXURES

PROFORMA

TO COMPARE THE EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POSTOPERATIVE ANALGESIA

NAME: SEX:

AGE I.P NO

DIAGNOSIS: PROCEDURE:

PREOPERATIVE ASSESSMENT:

HISTORY:

COMORBID CONDITIONS:

H/O PREVIOUS SURGERY:

DRUG ALLERGY:

GENERAL EXAMINATION:

HEIGHT: WEIGHT:

ANAEMIA: JAUNDICE:

PULSE RATE: SPINE:

BLOOD PRESSURE: CVS-

RS-

INVESTIGATIONS:

HB- BT,CT-

BLOOD SUGAR- BLOOD UREA-

CREATININE- ECG-

CXR-

TIME	ONSET	LEVEL ACHIEVED	VAS	DURATION	SIDE EFFECTS
BASELINE					
10 MIN					
30 MIN					
60 MIN					
90 MIN					
120 MIN					
150 MIN					
180 MIN					
210 MIN					
240 MIN					

SIDE EFFECTS	
NAUSEA,VOMITING	
PRURITUS	
SEDATION	
HYPOTENSION	
BRADYCARDIA	

INJ.EPHEDRINE (6 MG IV)

INJ.ATROPINE (0.6 MG IV)

RESCUE ANALGESIA

PATIENT CONSENT FORM

TO COMPARE THE EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING ELECTIVE HERNIOPLASTY

Study Centre : Department of Anaesthesiology & Critical Care, Kilpauk Medical College.

Participant Name : Age : Sex :

I.P. No :

I ,confirm that I have understood the purpose of procedure for the above study. I had the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure and the management of it. I have been explained about the safety, advantages and disadvantages of the techniques.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study.

I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study of "To COMPARE THE EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON POSTOPERATIVE ANALGESIA"

Name of the patient : Signature / thumb impression of patient :

Name of the witness : Signature :

Address : Contact Number :

Name of the Investigator : Signature :

Time : Date :

Place :

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COMPARING

5**EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON** POST OPERATIVE **ANALGESIA**

– A DOUBLE BLINDED RANDOMIZED STUDY Dissertation submitted in partial fulfillment for the award of M.D DEGREE EXAMINATION M.D ANESTHESIOLOGY & CRITICAL CARE- BRANCH X KILPAUK MEDICAL COLLEGE

19**SUBMITTED TO THE TAMILNADU DR.MGR MEDICAL UNIVERSITY CHENNAI**

APRIL-2013

19**CERTIFICATE This is to certify that this dissertation titled**

"COMPARING

5**EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON** POST OPERATIVE **ANALGESIA**

– A DOUBLE BLINDED RANDOMIZED STUDY" has been prepared by Dr. J.SURESH under my supervision in the Department of Anesthesiology, Government Kilpauk Medical College, Chennai during the academic period 2010-2013 and is being

19**submitted to the** Tamil Nadu **Dr.MGR Medical University, Chennai in partial fulfillment of the University** regulation **for the award of Degree of**

Doctor of Medicine (M.D Anesthesiology) and his dissertation is a bonafide work. Prof.P.Ramakrishnan, M.D.(Bio),DLO Prof.S.Gunasekaran,M.D.,D.A.D.N.B Dean Professor & HOD Govt. Kilpauk Medical College Department of Anesthesiology & Hospital Govt. Kilpauk Medical College Chennai & Hospital Chennai DECLARATION I, Dr. J.Suresh solemnly declare that the dissertation , "COMPARING

5**EFFICACY OF EPIDURAL DEXAMETHASONE VERSUS FENTANYL ON** POST OPERATIVE **ANALGESIA**

– A DOUBLE BLINDED RANDOMIZED STUDY" is a bonafide work done by me in the

2**Department of Anesthesiology and Critical care,** Government Kilpauk **Medical**

College& Hospital, Chennai under the guidance of Prof.S.Gunasekaran, M.D.,D.A,.D.N.B.,, Professor and HOD, Department of Anesthesiology, Government Kilpauk Medical College, Chennai-10. Place: Chennai-10 Signature Date: (J.SURESH) ACKNOWLEDGEMENT I wish to express my sincere thanks to Prof.P.Ramakrishnan, M.D.(Bio), D.L.O. Dean, Governmen Kilpauk Medical College& Hospital, Chennai for giving Ethical committee clearance and permitting me to utilize the facilities of the hospital for the conduct

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> 36**that occurs during surgery** can be attenuated **through reduction of** transmission of **nociceptive input** to **the central nervous system**

by providing perioperative analgesia. This also - Decreases complications, -Facilitate

> 36**recovery during the immediate postoperative period,**

-Improves long term recovery, -Reduces the length of hospital stay, -Improves the quality of life. (1) Post operative pain management should be planned and tailored to the needs of special population like ambulatory surgical patient, elderly, paediatric, opioid tolerant, obese patients and those with obstructive sleep apnea syndrome. IMMEDIATE EFFECTS OF POSTOPERATIVE PAIN:

> 22**Transmission of nociceptive stimuli from the periphery to the** Central nervous system **results in the neuroendocrine stress response,** a combination **of local inflammatory substances**

(eg.cytokines, prostaglandins, leukotrienes, tumor necrosis factor-α) and systemic mediators of the neuroendocrine response. Suprasegmental reflex response to pain results in

> 29**increased sympathetic tone,** increased **catecholamine** levels, **increased catabolic hormone secretion**

and decreased secretion of anabolic hormones which results in

> 29**sodium and water retention , increased levels of blood glucose, free fatty acids, ketone bodies and lactate.**

A hypermetabolic state occurs as metabolism and oxygen consumption are increased. The

> 13**extent of the stress response is** influenced **by** following **factors: ‣ the type of**

anesthesia, ‣ the degree of surgical trauma. The stress response may lead to postoperative hypercoagulability. Enhancement of coagulation, inhibition of fibrinolysis, increased platelet reactivity and plasma viscosity may contribute to an increased incidence of postoperative hypercoagulablility related events such as deep venous thrombosis, vascular graft failure and myocardial ischemia. The stress response also potentiate postoperative immunosuppression, the extent of which correlates with the severity of surgical injury. Sympathetic activation may increase

22**myocardial oxygen consumption, decrease myocardial oxygen supply through coronary vasoconstriction and attenuation of local metabolic coronary vasodilation.**

Activation of the sympathetic nervous system also delays return of postoperative gastrointestinal motility, which may develop into paralytic ileus (2) Postoperative respiratory function is markedly decreased, especially after upper abdominal and thoracic surgery. Reflex inhibition of phrenic nerve activity is an important component of this decreased postoperative pulmonary function.

13**Patients with poor pain control may breathe less deeply, have an inadequate cough, and** more susceptible **to**

the development of postoperative pulmonary complications. DELAYED EFFECTS OF POSTOPERATIVE PAIN: Chronic postsurgical pain [CPSP] is a largely unrecognized problem that may occur in 10% to 65% of postoperative patients.

23**Poorly controlled acute postoperative pain may be an important predictive factor in the development of**

CPSP. The transition from acute to chronic pain occurs very quickly and longterm behavioral and neurobiologic changes occur much earlier than was previously thought. CPSP is relatively common after procedures

23**such as limb amputation (30%** to 83%), **thoracotomy (22%** to 67%), **sternotomy**

(10 to 27%), and breast surgery (11% to 57%). Traditionally various techniques and drugs have been adopted for postoperative analgesia. These include regional techniques like epidural analgesia with local anesthetics alone or opioid alone or combination of both, peripheral blocks, NSAIDS, parenteral opioids, non epidural analgesia like intrapleural analgesia, paravertebral block, intra articular analgesia etc. Epidural steroids have been used successfully for long time for chronic pain syndrome. The safety of epidural steroids is well established. Based on the above evidences and concepts in this study we used dexamethasone epidurally to study the effects on postoperative pain relief. HISTORY OF EPIDURAL ANESTHESIA & ANALGESIA ‣ Jean Enthuse Sicard (1872-1929) and Fernand Cathelin (1873-1945) independently introduced cocaine through the sacral hiatus in 1901 ,thereby becoming the first practitioners of caudal (epidural) anesthesia. ‣ Sicard - a neurologist, used the technique to treat sciatica and tabes, but Cathelin used the technique for surgical anesthesia. ‣ Arthur Läwen (1876-1958)- an early proponent of regional anesthesia, successfully used caudal anesthesia with large volumes of procaine for pelvic surgery. ‣ Heile - published an extensive study of the epidural space in 1913. His unique approach was to enter the epidural space through the intervertebral foramina. ‣ In 1921, Fidel Pagés (1886-1923), a Spanish military surgeon- devised a technique to introduce epidural procaine at all levels of the neuraxis. His method was to use a blunt needle and then feel and hear entry of the needle through the ligamentum flavum. ‣ An important innovation was Dogliotti's method of identification of the epidural space. His textbook illustrates the use of continuous pressure on the plunger of a saline filled syringe as the needle is advanced through the ligamentous structures. ‣ Gutierrez of Argentina developed the “hanging drop” sign, which is still used by some anesthesiologists to identify the epidural space. William T. Lemmon (1896-1974) used a 17-gauge, malleable, silver needle that was connected through a hole in the operating room table to rubber tubing and a syringe. ‣ Edward B. Tuohy (1908-1959) used a ureteral catheter threaded through a large Huber-tipped spinal needle to provide continuous spinal anesthesia. ‣ Behar in 1979 first reported the use of epidural morphine for treatment of pain. ‣ Robecchi and Capra in 1952 treated radiculopathy

18**with periradicular hydrocortisone.** It **is the first documented use of epidural steroids**

. ANATOMY OF EPIDURAL SPACE Everything outside the dural sac but within the vertebral canal can be considered to constitute the epidural space. Boundaries of epidural space: ? The walls of vertebral canal including the vertebral bodies and discs anteriorly ? Pedicles laterally ? Lamina and ligamentum flava posteriorly Epidural space is a potential space normally contains – fat, vessels and nerves. The cranial epidural space is entirely empty. The epidural fat which is nearly fluid in texture permits gliding movement of the neural structures and provides a padding effect. The distribution of epidural contents is highly non uniform. Separated by these empty areas, the epidural contents occur as a series of metamerically and circumferentially discontinuous compartments. In contrast to this below L4, the dural sac tapers resulting in

complete filling of epidural fat. Thus there will be difficulty in delivering local anaesthetic to the L5 and sacral nerve roots during epidural anaesthesia, since solution is not confined in close proximity with neural structures at these levels. Posterior epidural compartment: A triangular part of fat pad fills the dura posterior to epidural space. It is enclosed by ligamentum flava but also extends under the caudal most portion of lamina above. The largest posterior epidural compartment is at the mid lumbar level with progressive decrease in anteroposterior dimension at thoracic levels (3) . Rostral to C7 level the posterior epidural space vanishes and the posterior dura lies in contact with the ligamentum flavum and the laminar bone. A cleft like space between epidural fat and the canal wall allows passage of catheters and injected fluids with only a minor impediment in posterior midline. This arrangement of opposing non adherent tissue plane is ideally designed to demonstrate the normal subatmospheric pressure within tissues, generated by the usual action of lymphatics and the balance of osmotic and hydrostatic forces across the capillary endothelium. Lateral epidural compartment: No epidural contents exist lateral to the dural sac where it is in contact with the vertebral pedicles. This compartment

7**forms just medial to each intervertebral foramen**

and is filled with segmental nerves, vessels and fat. The

7**pressure in the epidural space closely reflects abdominal pressure**

because of the flexibility of tissues and lack of rigid barrier.

7**Increased abdominal pressure such as during a cough or pregnancy is** therefore **readily transmitted to the epidural space.**

Anterior epidural space:

7**The anterior epidural compartment is separated from rest of** vertebral column **by**

fascia of posterior longitudinal ligament. The spread of injected drug anterior to plane of posterior longitudinal ligament is effectively blocked by this membrane.At the level of the narrow mid portion of the vertebral body this is almost occupied by internal vertebral plexus. Catheters that transgress into the anterior epidural space through the fascia of the posterior longitudinal ligament are likely to enter the venous plexus. Functional implications of epidural space: The spread of injected solutions is circumferential at a given level and passes out of the intervertebral foramen and likewise freely passes longitudinally within the vertebral canal. As the catheter is advanced through the needle, there may be a brief resistance to advancement as the tip encounters the dura. CT scan shows that

7**catheter tip inserted 3 cm into the** vertebral **canal**

most commonly travel laterally to the internal aspect of an intervertebral foramen because of the stiffness of the short segment of catheter that has emerged from the needle.

7**Even when the catheter tip lies exterior to the intervertebral** foramina **in the paravertebral space,** the **distribution of the** injected solution **is preferentially back into the** vertebral **canal**

. PHYSIOLOGICAL EFFECTS OF EPIDURAL BLOCKADE Epidural neural blockade implies sympathetic blockade accompanied by somatic blockade in the form of sensory and motor blockade alone or in combination. CARDIOVASCULAR EFFECTS: Blockade of sympathetic innervation accounts for the cardiovascular responses. Preganglionic sympathetic innervation – regulates regional blood flow. Post ganglionic sympathetic innervations – controls cardiac function and vascular tone. Peripheral sympathetic blockade causes vascular dilatation in pelvis and lower limbs when lower thoracic and lumbar segments are blocked with epidural anaesthesia. Cardiovascular depression is atleast partly related to the level of sympathetic blockade. Vascular absorption of local anaesthetic and addition of vasoconstrictor may result in significant hemodynamic changes after epidural but not after subarachnoid blockade. Lumbar epidural anaesthesia with sympathetic blockade below T10 results in minimal vasodilatory consequences because fewer vasoconstrictor fibres are included and neither the sphlanchnic nerves nor the nerve supply to the adrenal medulla are affected. Since muscle veins lack sympathetic innervation, venodilatation of the extremities is limited to skin and so minimal capacitance increase results from blocks of the lower

extremities .(4) .Lumbar epidural anesthesia with a sympathetic blockade extending to the lower segments may occasionally be associated with profound bradycardia and circulatory collapse without any obvious precipitating event. EFFECTS ON RESPIRATION: Following aspects may influence respiration. ‣ sensory neural blockade reduces nociceptive afferent drive to respiratory center. ‣ motor neural blockade of intercostals muscles, abdominal muscles and diaphragm. ‣ sympathetic neural blockade with resultant change in cardiac output . ‣ vagal dominance. The potential for phrenic nerve palsy is rare with epidural block. Respiratory arrest is rare and commonly associated with extensive sympathetic blockade, reduced cardiac output and reduced oxygen to the CNS. In patients with severe pain epidural block probably improves Vital capacity and Functional residual capacity as well as PaO2. Thoracic epidural anesthesia does not impair the hypoxic drive. The inhibitory reflex of phrenic nerve motor drive is interrupted with thoracic epidural anesthesia resulting in increased diaphragmatic activity . NEUROENDOCRINE EFFECTS OF EPIDURAL BLOCKADE: Most of the surgically induced endocrine and metabolic changes are

48**abolished by an appropriate level of sensory blockade produced by regional anesthesia.**

Surgical stress responses during major upper abdominal and thoracic procedures are not effectively amileorated by epidural anaesthesia due to incomplete blockade of nociceptive pathways. Sympathetic block abolishes the increase in renin activity in response to arterial hypotension. Vasopressin system is activated in response to hypotension EPIDURAL BLOCKADE AND MOTOR FUNCTION: The degree of motor blockade increases as dose of drug increases. Usage of dilute concentration of local anesthetics facilitates ultra early ambulation. Motor blockade in lower limbs is assessed by bromage scale.

20**BROMAGE SCALE: No block (0%)** Partial (33%) **Full flexion of knees and feet possible Just able to flex knees, still full flexion of feet possible** Almost complete(66%) **Unable to flex knees, still flexion of feet** Complete (100%) **Unable to move legs or feet**

Table 1 showing assessment of motor blockade in lower limb RECTUS ABDOMINIS MUSCLE (RAM) TEST: This is useful in abdominal surgery, when abdominal muscle blockade is required rather than lower limb muscle blockade. (5) 100% power Able to rise from supine to sitting position with hands behind head 80% power Can sit only with arms extended 60% power Can lift only head and scapula off bed 40% power Can lift only shoulders off bed 20% power An increase in abdominal muscle tension can be felt during effort; no other response Table 2 showing assessment of motor blockade of abdominal muscles. THERMOREGULATION AND SHIVERING: Hypothermia is common in patients undergoing surgery with epidural anesthesia and it results from heat loss to the cold environment due to sympathectomy induced vasodilatation and in part from redistribution of heat from central to peripheral regions. Pregnancy may enhance the contribution of spinal thermoregulatory input. Injection of epidural pethidine 25mg or epidural fentanyl 50 µg abolishes shivering from epidural local analgesia. EFFECTS ON GIT: Epidural block extending from T6 to L1 effectively denervates the sphlanchnic sympathetic supply to the abdominal viscera. As a result parasympathetic activity predominates resulting in contraction of gut. Thoracic epidural anesthesia with local anaesthetics shortens the duration of postoperative paralytic ileus. Unopposed parasympathetic activity with blockade of afferent nociceptive and thoracolumbar efferents produces a shortened postoperative colonic ileus. Epidural anesthesia have protective action on gut due to improved mucosal blood flow. This increase in blood flow may contribute to the healing of gut anastomosis. Epidural anesthesia with local anaesthetic seems to be the best method for relieving pain after gastrointestinal surgery. EFFECTS ON BLOOD LOSS: Patients receiving epidural block had operative blood losses that were half those associated with general anaesthesia. Blood loss can be reduced as far as 30 to 40 % if epidural block is used for hip surgery. Factors that reduce blood loss include mild reduction in arterial blood pressure, increase in venous capacitance, prevention of high venous pressure in response to sympathetic activity resulting from pain and use of appropriate position. EPIDURAL ANESTHESIA & ANALGESIA Epidural anesthesia is a central neuraxial block technique which provides segmental blockade.

1**Improvements in equipment, drugs and technique have made it a popular and versatile** anesthetic **technique, with applications in surgery, obstetrics and pain control.**

1**Its versatility means it can be used as an** anesthetic, **as an analgesic adjuvant to general** anesthesia, **and for postoperative analgesia in procedures involving the lower limbs, perineum, pelvis, abdomen and thorax. Indications: General: Epidural** anesthesia **can be used as sole** anesthetic **for procedures involving**

the lower limbs, pelvis, perineum and lower abdomen. It is possible to perform upper abdominal and thoracic procedures under epidural anesthesia alone, but the height of block required, with its attendant side effects, make it difficult to avoid significant patient discomfort and risk. The advantage of epidural over spinal anesthesia is the ability to maintain continuous anesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration. This feature also enables the use of this technique into the postoperative period for analgesia, using lower concentrations of local anaesthetic drugs or in combination with different agents. Specific uses Hip and knee surgery: Internal fixation of a fractured hip is associated with less blood loss when central neuraxial block is used. The rate of deep venous thrombosis is reduced in patients undergoing total hip and knee replacement, when epidural anaesthesia is used. Vascular reconstruction of the lower limbs: Epidural anesthesia improves distal blood flow in patients undergoing arterial reconstruction surgery. Amputation: Patients given epidural anaesthesia 48-72 hours prior to lower limb amputation may have a lower incidence of phantom limb pain following surgery.

1Thoracic trauma with rib or sternum fractures: Adequate analgesia in patients with thoracic trauma improves respiratory function by allowing the patient to breathe adequately, cough and cooperate with chest physiotherapy.

1Obstetrics: Epidural analgesia is indicated in obstetric patients in difficult or high-risk labour.

1Caesarean section performed under central neuraxial block is associated with a lower maternal mortality

and better perioperative outcome. CONTRAINDICATION OF EPIDURAL ANESTHESIA: ABSOLUTE: ?

34Patient refusal ? Infection at the site of injection ? Coagulopathy or other bleeding diathesis ? Severe hypovolemia ? Increased intracranial pressure ? Severe stenotic valvular heart disease RELATIVE:

? Sepsis ? Uncooperative patient ? Pre-existing neurological disease ? Severe spinal deformities ADVANTAGES: ‣

4Use of perioperative epidural anesthesia and analgesia, especially with a local anesthetic–based analgesic solution, can attenuate the pathophysiologic response to surgery and may be associated with a reduction in mortality and morbidity when compared with analgesia with systemic opioid agents. Use of epidural analgesia can decrease the incidence of postoperative gastrointestinal, pulmonary, and possibly cardiac

complications

4by inhibiting sympathetic outflow, decreasing the total opioid dose, and attenuating spinal reflex inhibition of the gastrointestinal tract.

‣ Postoperative thoracic epidural analgesia can

10facilitate return of gastrointestinal motility without contributing to anastomotic bowel dehiscence. Patients who receive epidural local

anesthetics have

> 13**an earlier return of gastrointestinal motility** after **abdominal surgery.**

,

> 4**Perioperative use of epidural analgesia with a local anesthetic–based regimen in patients undergoing abdominal and thoracic surgery**

decreases

> 4**postoperative pulmonary complications, presumably by preserving** postoperative **pulmonary function by providing superior analgesia and**

thus reducing splinting behavior

> 4**and attenuating** the **spinal reflex inhibition of** diaphragmatic **function.**

,

> 42**Use of** postoperative **thoracic, but not lumbar epidural analgesia** may decrease **the incidence of postoperative myocardial infarction**

(12) ,possibly

> 13**by attenuating the stress response hypercoagulability, improving postoperative analgesia and providing** favorable **redistribution of coronary blood**

flow. FACTORS AFFECTING EPIDURAL BLOCKADE: SITE OF INJECTION AND NERVE ROOT SIZE: Injection of drug close to nerve roots results in rapid and intense blockade. After lumbar epidural injection, a somewhat greater cranial than caudal spread of analgesia occurs. The spread of analgesia is even when drugs are injected in midthoracic epidural injection. Concentration of large number of nerve fibres within upper thoracic and cervical segments makes them resistant to blockade with epidural injections. Caudal epidural block spreads from S5 and the S1 segment is the last to be blocked. AGE: In the elderly, the areolar tissue around the intervertebral foramina becomes dense and firm partially sealing the foramina. The permeability of duramater increases with increase in age. Aging is associated with reduced beta adrenergic responsiveness.

> 2**Increased levels of analgesia with** increase in **age have been attributed to** : ‣ Progressive sclerosis **of**

intervertebral foramina results in reduced leakage of injected solutions into paravertebral space. ‣ Increased permeability of duramater. ‣ Increased compliance of the epidural space. ‣ Decreased resistance of epidural space. With aging neural population declines steadily within the spinal cord and peripheral nerves show a linear reduction in conduction velocity especially motor nerves. These changes makes older patients more sensitive to local anesthetics with altered motor block profile. Thermoregulatory response declines with age as shown by decrease in core temperature consequently rewarming process will occur more slowly in elder patients. POSITION OF THE PATIENT: Comparison of sitting and lateral position for epidural block reveals no significant differences in cephalad spread. An exception is the obese patient who achieves a lower level of block when seated. The spread of analgesia is more intense in dependent portion when drugs injected in lateral position in both pregnant and non pregnant women. Motor and sensory block onset will be rapid in the dependent portion. SPEED OF INJECTION: Rapid injection of local anesthetics into epidural space has no effect on spread of analgesia and has only minimal effect on bulk flow of solution in the space. Rapid injections of large volumes of solution may increase CSF pressure, decreases spinal cord blood flow, increase intracranial pressure and pose a risk of spinal or cerebral complications. Headache is commonly reported if epidural solutions are rapidly injected. CONCENTRATION AND DOSE OF LOCAL ANAESTHETIC: Below concentrations of 1% lignocaine motor block is minimal regardless of dose, unless injections are repeated at intervals. When dilute solutions in

concentration of 0.125% or 0.625% are injected repeatedly the intensity of sensory and motor blockade increase. This mechanism is particularly important in obstetric analgesia. Increasing concentration results in reduction in onset time yet produces intense motor blockade. DRUG CLINICAL CONCENTRATION DURATION(min) USE (%) Lignocaine infiltration 0.5 - 1 60 - 240 epidural 1.5 - 2 60 - 120 spinal 1.5 - 5 30 - 60 Bupivacaine infiltration 0.25 120 - 480 epidural 0.5 – 0.75 120 - 300

44**spinal 0.5 – 0.75** 60 - 240 Ropivacaine **infiltration 0.**

2 – 0.5 120 - 360

44**epidural 0.5 - 1** 120 - 360 spinal **0.** 5 – **0.**

75 90 - 200 Table 3 showing concentration of commonly used drugs. If more potent analgesia with minimal motor block is required 0.5% bupivacaine, 0.5% ropivacaine, 0.5% levobupivacaine or 1% lignocaine may be chosen. The requirement of profound sensory block and excellent muscle relaxation are best met by 1% lignocaine with epinephrine or 0.75% to 1% ropivacaine. The toxic plasma concentration of lignocaine, bupivacaine, ropivacaine were >5, > 3, >4 ng / ml respectively. ADJUVANTS: EPINEPHRINE: When freshly prepared epinephrine in a concentration of 1:2,00,000 is added to the local anaesthetic solution , it ‣ Improves the quality of sensory block. ‣ Increases the duration and intensity of motor blockade. Enhancement of analgesia seen with epinephrine is due to activation of dorsal horn inhibitory system via α 2 adreno receptor and to some extent through decreased vascular absorption. CLONIDINE: It is a selective α 2 adrenergic agonist which acts by

2**opening potassium channels.** Prolongs **duration of both sensory and motor blockade**

by synergistic action with local anaesthetics. Side effects: ? Arterial hypotension-

2**due to direct inhibition of sympathetic outflow** from pre ganglionic **neurons in the spinal cord,**

? reduction in heart rate . KETAMINE: It

2**blocks the calcium channel on the NMDA**

(N- methyl D aspartate) receptor complex and decreases depolarisation by inhibiting excitatory transmission. NEOSTIGMINE: The cholinergic system modulates pain perception by a spinal mechanism.

2**Analgesia by neostigmine is associated with**

8**high incidence of nausea and vomiting.** NUMBER & FREQUENCY **OF**

LOCAL ANESTHETIC INJECTIONS: A single repeat dose (20% of total dose) given approximately 20 minutes after the main dose of local anaesthetic has been said to consolidate blockade within the level of blockade already established. Thus missed segments may be filled in but the level of blockade may not be extended. A second dose of approximately 50% of initial dosage will maintain the initial segmental level of analgesia if given when the upper level of segmental analgesia has receded 1 to 2 dermatomes. In addition tachyphylaxis increases with the number of injections especially when short acting amides are used. PHYSIOLOGY OF PAIN PAIN:

25**International association for study of pain has defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or defined in terms of such damage.**

There are two components of pain. Neurophysiologically mediated sensory component and an emotional component. There are two types of pain 1. Physiological pain is a transient sensation due to noxious mechanical, thermal, chemical stimulus each with a clearly defined threshold and without causing damage to the nervous system. 2. Pathological pain is an inflammatory response to tissue injury or damage to central nervous system with an alteration in perception. Pain following surgery is pathological. There are

two major theories of pain. 1. Specificity theory proposed by Von Frey states that pain is due to stimulation of specific end organs. 2. Intensive / Summation / Pattern theory proposed by Gold Scheider states that there are no specific pain receptors and any sensory stimulus if sufficiently severe would produce pain. ORGANISATION OF PAIN PATHWAYS: According to the recent theory, pain pathway is organized as follows RECEPTORS: Nociceptive receptors are fine, profusely branched, free nerve endings covered by Schwann cells with little or no myelin. They are present in skin, viscera and other organs. There are three types of receptors 1. Mechanosensitive nociceptors activated by mechanical stimuli. 2. Mechanothermal nociceptors activated by mechanical and thermal stimuli >43ºC. 3. Polymodal pain receptors respond to mechanical, thermal and chemical stimuli like hydrogen, potassium ions, histamine, serotonin, prostaglandins. FIRST ORDER NEURONS: Mechanosensitive and mechanothermal pain receptors transmit impulses through thinly myelinated A δ fibres of 1-5 μ diameter with conduction velocity of 15-30 metres per second. This is responsible for fast pain which is sharply localized. Polymodal pain receptors transmit impulses through unmyelinated C fibres of 0.4-1.1 μ diameter with conduction velocity of 0.5 – 2 meters per second. This is responsible for the poorly localized slow pain. Transmission through both these fibres causes the " Double response of Lewis". The peripheral afferent fibres have their

2**cell body in the dorsal root ganglion** and project via **the**

lateral part of the dorsal root called " Tract of Lissauer". They terminate in dorsal horn of spinal cord within 1 to 2 segments of entry. A δ fibres terminate in lamina 1 (marginal cell layer of Waldeyer) and lamina 5 (wide dynamic range of neurons which respond to other modalities also). Unmyelinated C fibres terminate in lamina 2 and 3 (substantia gelatinosa). SECOND ORDER NEURONS: They arise from the cell and

37**connect with ventral and lateral horn cells in the same and adjacent spinal segments** which subserve both **somatic and autonomic reflexes.**

Around 75% of other sensory neurons project contralaterally after decussating in the anterior commissure 1-3 segments higher than the root of entry and divide into two ascending tracts. Neospinothalamic / Lateral spinothalamic tract: It ascends in the anterolateral funiculus of spinal cord to brain stem and thalamus. It contains fast conducting fibres which transmit specific localised pain, identifiable in quality and intensity causing "First Pain ". The fibres are arranged in such a way that fibres from lower part of the body are superficial and from upper part of the body are innermost. Palaeospinothalamic / Ventral spinothalamic / Spinoreticulothalamic tract: It is medially placed and contains slowly conducting fibres responsible for "Second Pain" and has connections with brainstem, limbic and subcortical regions. Thalamic terminus: Most of the fibres of spinothalamic tract terminate in the nucleus ventro posterolateralis which is the major sensory relay nucleus. The other fibres terminate in the posterior group of nuclei, ventrobasal complex and hypothalamic nuclei. THIRD ORDER NEURONS / THALAMOCORTICAL PROJECTIONS: Posterior thalamic nuclei project to the post central cortex and upper bank of sylvian fissure and subserve tactile and proprioceptive stimuli with discriminative sensory function. Pain afferents received from mesencephalic offset of anterolateral funiculus project to the amygdaloid nuclei and other areas related to affect the emotion. PERCEPTION OF PAIN : The threshold for the perception of pain is the lowest intensity of stimulus recognized as pain. The conscious awareness or perception of pain occurs at the thalamic level and thalamic pain occurs when the thalamocortical pathway is destroyed. Somatosensory cortex is essential for the accurate localization, appreciation of intensity and other discriminative aspects of pain. Prefrontal cortex subserves the unpleasant affective and emotional reaction to pain. GATE CONTROL THEORY OF PAIN: It was propounded by Melzack and Walls in 1965. It states that modulation of pain impulses in the dorsal horn can control further synaptic transmission via the spinothalamic tract. It states that stimulation of large afferent fibres excite the I cells (inhibitory cells) in the lamina 2 and 3 of dorsal horn which in turn cause pre and post synaptic inhibition of secondary transmission neurons (T cells) in lamina 5 of dorsal horn and interrupt pain pathway. Conversely stimulation of small pain afferents (C fibres) inhibit the I cells leaving the T cells in the excitatory state thus facilitating transmission of pain. Endogenous opioids and spinal modulation of pain perception: Hughes et al described endogenous morphine like substances with analgesic activity called endorphins. There are 5 endorphins, ? Metenkephalin, ? Leuenkephalin, ? Betaendorphin, ? L endorphin ? R endorphin. Metenkephalin and Leuenkephalin: They are inhibitory neurotransmitters at the primary afferent nociceptive site. They act through release of substance P. Dynorphins: Control nociception at the spinal cord level through activation of kappa receptors. It is present in lamina 1 to 5 of dorsal horn. L-endorphin and R- endorphins : Breakdown products of beta endorphins. PHARMACOLOGY OF OPIOIDS Opium is extracted from the capsule of a poppy plants (Papaver somniferum). It is a brown residual material and has two active alkaloid ingredients, phenanthrene derivatives and benzoisoquinoline derivatives. Morphine, codeine and thebaine are derivatives of the former while papaverine and noscapine are derivatives of the latter compound. Morphine is naturally available at 10% concentration in wild poppy. μ 1 μ 2 κ δ EFFECT Analgesia Analgesia(spinal) Analgesia Analgesia Euphoria Depression of ventilation Dysphoria Depression of ventilation Miosis Constipation Miosis Constipation Table 4 shows classification of opioid receptor LOCATION OF OPIOID RECEPTORS: Opioid receptors are located in the areas of brain (periaqueductal gray matter of brainstem, amygdale, corpus striatum, hypothalamus) and spinal cord (substantia gelatinosa) that are involved in pain perception, integration of pain impulses and responses to pain. Mu

(μ) Delta (δ) Kappa (κ) Fentanyl +++ +++ +++ Morphine +++ + Sufentanil +++ + + Nalbuphine ++ Butarphanol +++ Table 5. shows agonist effects of drugs on specific receptors Classification of opioids: Natural opioids: Morpine, Codeine Semisythetic opioids: Diacetylemorphine and Pholcodine Synthetic opioids: Pethidine, Fentanyl, Methdadone, Tramadol Drug analgesia Respiratory Antitussive constipation Dependence depression effect liability Mixed Opioid Agonist antagonist Pentazocine +++ ++ 0 + + Butarphanol +++ ++ 0 + + Nalbuphine +++ ++ 0 + + Buprenorphine +++ ++ + ++ + General Pharmacological Actions of opioids: Analgesia: Morpine is the most efficacious analgesic. The analgesia is dose dependent. Dull visceral pain is better relieved than sharp somatic pain. The degree of analgesia is dose dependent. At high doses it can relieve even very sharp somatic pain and to a very high degree. It

2**is most effective** at **relieving** nociceptive **pain arising from** stimulation **of**

nerve endings compared to neuropathic pain. Intrathecal injection has been shown to cause segmental analgesia without affecting other modalities of sensation, while in the spinal cord it acts directly on the substansia gelatinosa to inhibit release of excitatory neurotransmitters from the afferent fibres. Sedation: Indifference to self and surroundings accompanied by drowsiness occurs. This differs from hypnotics in that there is no motor incoordination involved. With increase in dose, sleep and coma can occur. Respiratory center: The respiratory center gets depressed and both rate and tidal volume are affected. Multiple instances of death due to overdose have been recorded. In addition to depression of the respiratory center, there is indifference to breathing by the apneic patients themselves. They may not breath unless commanded to do so. Mood and other subjective effects: Opioids have a calming effect on the general population. There is loss of apprehension and a feeling of detachment. There is a lack of initiative and mental clouding. All of these are perceived as unpleasant sensations in the absence of pain. The feeling of detachment is described as “floating” by addicts. Cough center: The cough center is affected more than the respiratory center. Cough reflex is suppressed severely even at low doses. This is being used in cough suppressants like codeine. Cardio-vascular system: Morphine causes differential vasodilation which is greater in the systemic circuits compared to the pulmonary circuits resulting in a shift of blood to the systemic circulation. The vasodilation is mediated by multiple mechanisms including release of histamine, a direct depressant action on the vasomotor center and a direct action on the tone of the vessels. This results in overall reduced cardiac output due to the decreased peripheral resistance. Neuroendocrine system: Hypothalamic afferent collaterals are suppressed. There is universal suppression of all neuro-endocrine secretion. The posterior pituitary is affected more than the anterior pituitary. But these effects are short-lived and tolerance develops to these effects immediately. (7) GIT: Constipation is a major result of the action of morphine. There is increased tone and segmentation movements but decreased propulsive movements. Spasm of pyloric, ileocaecal and anal sphincters can occur. There is also central action causing inattention to defecation reflex. Other smooth muscles: Morphine causes spasm of the sphincter of Oddi. This can result in increased biliary pressure and biliary colic. The tone of both detrusor and the sphincter is increased resulting in difficulty in micturition and a feeling of urgency. It may slightly prolong labor and cause significant broncho constriction in asthmatics due to the release of histamine. Pharmacokinetics: A high and variable first-pass metabolism results in poor oral absorption of morphine with only about 20-25% bioavailability. There is a very high amount of distribution in the tissues compared to the plasma resulting in a high volume of distribution. The half-life of the drug ranges from 4-6 hours because of the extensive tissue distribution. Adverse Effects: Dysphoric effects like sedation, lethargy and clouding of cognition can occur. Vomiting, constipation and respiratory depression are common even at low therapeutic doses. Blurring of vision and urinary retention can occur in the elderly. Hypotension can occur in mobile patients. Allergic reactions have been reported but are few and far between. Local reactions at the sites of injections are more common . Dependence and Tolerance: Morphine exhibits a high degree of tolerance.Tolerance occurs for all actions except constipation and miosis.Subjects tolerant to morphine exhibit tolerance to most CNS depressants as well. Withdrawal leads to drug seeking behavior in patients. Physical manifestations seen are mostly the opposite of the effects – lacrimation, sweating, diarrhea, mydriasis, hyperventilation, vasoconstriction and if prolonged weight loss and suicidal tendencies. Interactions: Tricyclic anti-depressants, Mono-amine oxidase, phenothiazine, amphetamines and neostigmine potentiate the effect of morphine. Morphine in turn retards the digestion of drugs by delaying gastic emptying. NALOXONE: Pure opioid receptor antagonist. Recommended dose is 0.4 – 0. Mg. When carefully titrated and administered it often restore spontaneous ventilation without reversal of adequate analgesia. Onset of action is 1 – 2 minutes with half life of 30 – 60 minutes. NALTREXONE: Pure opioid antagonist, long acting than naloxone. Duration of action is 30 – 90 minutes. Effective oral prophylactic against pruritus and vomiting associated with intrathecal morphine. FENTANYL Structural formula of fentanyl

15**Synthetic opioid related to the** phenylpiperidines. **The actions of fentanyl**

is similar to those of μ-receptor agonists. PHARMACOLOGICAL PROPERTIES 100

15**times more potent than morphine, most commonly administered**

intravenously, can be administered through epidural, intrathecal, transdermal and, oral route. The

> 45**plasma concentration of fentanyl required for** postoperative **analgesia was approximately 1.5 ng / ml**

(8) The advantage of liphophiicity is that the risk of delayed respiratory depression is less when compared with morphine . The

> 15**time to peak analgesic effect after intravenous administration** is 5 minutes. **Fentanyl**

has high degree of cardiac stability due to less effect on heart rate and blood pressure, minimal myocardial depression with no release of histamine.

> 15**High doses of fentanyl or sufentanil are commonly used as the primary anesthetic for patients undergoing cardiovascular surgery.**

fentanyl As Analgesic As infusion For induction Dose 2 – 6 µg / kg 0.5 – 5 µg / kg / hr 4 – 20 µg / kg Table 7 showing various dosage of fentanyl PHYSIOCHEMICAL PROFILE: Molecular weight 528.29 pKa 8.4 % unionized at pH 7.4 8.5% % bound to plasma proteins 84% Potency 100 > than morphine Table 8 showing physiochemical properties of fentanyl PHARMACOKINETIC PROFILE: Volume of distribution at steady state 335 litres Clearance 1530 ml / minutes Effect site equilibration time 6.8 minutes Hepatic extraction ratio 0.8 – 0.1 Context sensitive half time 260 minutes Elimination half time 3.1 – 6.6 hours First pass pulmonary uptake 75% Table 9 showing pharmacokinetics of fentanyl PHARMACOLOGY OF STEROIDS Two classes of steroids: The corticosteroids, and androgens. The

> 16**corticosteroids are** classified **as glucocorticoid (carbohydrate** metabolism **– regulating) and mineralocorticoid (electrolyte** balance **–regulating).**

The important glucocorticoid and mineralocorticoid in human is cortisol and aldosterone respectively. GENERAL MECHANISMS FOR CORTICOSTEROID EFFECTS: Interaction

> 16**with specific receptor proteins in target tissues** upregulate **the expression of** corticosteroid **-responsive genes,** which changes **the levels and array of proteins synthesized by the various target tissues.** MOLECULAR MECHANISM **OF**

ANTI INFLAMMATORY EFFECTS OF GLUCOCORTICOIDS: Glucocorticosteroids are potent anti-inflammatory agents. This anti- inflammatory effect may be produced via a variety of mechanisms. A group of structurally related, calcium-dependent phospholipid-binding proteins, annexins, which were formerly known as lipocortins or calpactins, had been shown to be inducible by glucocorticoids. Annexin I has been reported to inhibit sPLA 2 activity in vitro. These observations led to the hypothesis that the inhibition of sPLA 2 by annexins is the mechanism of the anti-inflammatory action of glucocorticoids. (9) The

> 21**prolongation of analgesic duration** of perineural **administration of dexamethasone may be secondary to local action on nociceptive- C** fibres **mediated via** glucocorticoid **receptors and** upregulation **of function of potassium channels in excitable cells**

CARBOHYDRATE AND PROTEIN METABOLISM : Stimulation of glucose synthesis

> 16**from amino acids and glycerol and** storage **as glycogen in**

liver. There is diminished glucose utilisation with increased protein breakdown in the periphery resulting in increased blood glucose. Glycemic control can be worsen in patients taking corticosteroids. LIPID METABOLISM: Redistribution of body fat results in increased fat accumulation in supraclavicular area, nape of the neck, face along with a loss of fat in the extremities. An increase in free fatty acid level occurs due to augmentation of lipolytic effects of growth hormone and adrenergic agonists. ELECTROLYTE AND WATER BALANCE : In patients with glucocorticoid deficiency there is increased secretion of vasopressin, which stimulates water reabsorption in the kidney. Steroids interfere with Ca 2+ uptake in the gut and

increase Ca 2+ excretion by the kidney leading to decreased total body Ca 2+ stores. The most striking cardiovascular effects of corticosteroids result from mineralocorticoid-induced changes in renal Na+ excretion, leading to increased sodium and water retention in primary aldosteronism there is enhanced response to vasoactive drugs. SKELETAL MUSCLE: In Addison's disease, weakness , fatigue and diminished work capacity are the prominent symptoms. In primary aldosteronism weakness and fatigue occurs due to steroid myopathy. CENTRAL NERVOUS SYSTEM: Patients with adrenal insufficiency exhibit apathy, depression and irritability. Replacement therapy will alleviate such symptoms. Treatment with glucocorticoids may result in behavioural changes such as mania, insomnia and restlessness and these abnormalities disappear with cessation of therapy. BLOOD AND FORMED ELEMENTS: Corticosteroids exert minimal effects on erythrocytes and haemoglobin as evident by polycythemia in cushing syndrome, an normocytic normochromic anaemia in addisons disease. A single dose of hydrocortisone can decrease the circulating levels of these cells within 4-6 hours . This persists for 24 hours and it results from redistribution of cells away from periphery. PHARMACOLOGY OF DEXAMETHASONE: Structural formula of dexamethasone PHARMCOKINETICS OF DEXAMETHASONE Bioavailability 80 – 90 % Protein binding 70 % Metabolism Half life Excretion Molecular weight hepatic 36 – 54 hours renal 392.4 g / mol Table 10 showing pharmacokinetics of dexamethasone

> 5**Dexamethasone is a high potency, long acting glucocorticoid with little mineralocorticoid effect.** It **has been used** intravenously **for prophylaxis of postoperative nausea. Single doses of** epidural **dexamethasone and other glucocorticoids have been reported to improve analgesia after various**

surgeries.

> 6**Acute noxious stimulation of peripheral tissues leads to sensitization of dorsal horn neurons of the spinal cord by the release of excitatory amino acids such as glutamate and aspartate. These amino acids activate N-methyl-D- aspartate receptors resulting in calcium ion influx. As a result, increased intracellular calcium activates phospholipase A 2 which converts membrane phospholipids to arachidonic acid. Simultaneously, there is up-regulation of the expression of cyclo-oxygenase 2 in the spinal cord, leading to prostaglandin E 2 synthesis, which results in a**

hyperalgesia. MECHANISM OF ACTION OF EPIDURAL STEROIDS: Dexamethasone and other steroids act by suppression of

> 18**transmission in thin unmyelinated C fibres while not affecting myelinated Aβ fibres. It**

exerts these action through direct membrane stabilising effect and indirectly through mediators

> 18**.These direct and indirect actions lead to decrease in** intraneuronal edema **and venous congestion thereby reducing** ischemia **and improving pain.**

PHARMACOLOGY OF BUPIVACAINE It is an amide local anaesthetic first synthesized in Sweden by Ekenstam and his colleagues in 1957 and used clinically L.J.Telivuo in 1963. Its molecular weight is 288. It is an amide local anesthetic (

> 30**1-butyl- N-(2,6,** dimethyl phenyl **piperidine-2- carboxamide)**

Prepared as a clear solution of 0.25%, 0.5%, 0.75% solution of bupivacaine hydrochloride. The hyperbaric solution used for subarachnoid block contains 80 mg / ml of glucose.

> 9**MECHANISM OF ACTION: Local anesthetics such as bupivacaine block the generation** an **conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the** prolongation **of the nerve impulse and reducing the rate of rise of the action potential. The progression of anesthesia is related to the diameter, myelination and conduction velocity of affected nerve** fibres. **The**

30**analgesic effects are thought to be due to its binding to the prostaglandin E2 receptors.**

ROUTES OF ADMINISTRATION: May be administered topically by infiltration, intrathecally or epidurally. The therapeutic dose of bupivacaine is 2 – 3 mg / kg (with or without epinephrine). METABOLISM: The possible pathway for metabolism of bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Only the N- dealkylated metabolite N-desbutyl bupivacaine has been measured in the blood or urine.5 % of the dose is excreted in the urine as pipcolloxylidine.16 % is excreted unchanged. SYSTEMIC TOXICITY: CARDIOVASCULAR SYSTEM: Bupivacaine is markedly cardiotoxic. It binds to specific myocardial proteins. In toxic concentrations the drug decreases the peripheral vascular resistance and myocardial contractility producing hypotension and cardiovascular collapse. Cardiotoxic plasma concentration is 8 – 10 µg / ml. CENTRAL NERVOUS SYSTEM: During accidental overdosage or direct vascular injections the clinical signs are numbness of tongue, light headedness, visual and auditory disturbances, muscle twitching, tremors. The signs may progress to generalised convulsions of the tonic clonic nature. The typical plasma concentrations of bupivacainne associated with seizures is 4.5 – 5.5 µg / ml. PHARMACOKINETICS: At pH 7.4 only 15% exist in non ionised form. Absorption depends on the site of injection, dosage and use of epinephrine. pKa 8.1 Protein binding 95 % Lipid solubility 28 %

39**Volume of distribution Clearance of drug** from plasma **Elimination half** life Onset **time**

73 litre 0.471 litre / minute 210 minute 5 – 7 minute Table 11 showing pharmacokinetics of bupivacaine METHODS OF POST OPERATIVE ANALGESIA SYSTEMIC OPIOIDS: Parenteral

4**opioid analgesics are one of the cornerstone options for the treatment of postoperative pain.** These agents **generally** exert **their analgesic effects through**µ **-receptors in the CNS.**

Opioids may be administered by the subcutaneous, transdermal, transmucosal, or intramuscular route, but the most common routes of postoperative systemic opioid analgesic administration are oral and intravenous. Opioids may also be administered at specific anatomic sites such as the intrathecal or epidural space .

12**INTRAVENOUS PATIENT CONTROLLED ANALGESIA: Intravenous patient-controlled analgesia (PCA)**

optimizes delivery of analgesic opioids and minimizes

26**the effects of pharmacokinetic and pharmacodynamic variability** in **individual patients.**

4**Although some equipment related malfunctions have been reported, the PCA device itself is relatively free of** problems. **Most** of the **problems related to PCA use result from user or operator** error. **The**

26**lockout interval may also affect the analgesic efficacy of** intravenous **PCA.** In essence, the **lockout interval is**

a safety feature of intravenous PCA, and most

12**intervals range from 5 to 10 minutes.**

10**NON STEROIDAL ANTI INFLAMMATORY AGENTS: NSAIDs**

generally provide

39**effective analgesia for mild to moderate pain.**

NSAIDs are also traditionally considered a useful adjunct to

23**opioids for the treatment of moderate to severe pain.**

NSAIDs

12**may be administered orally or parenterally,** rectally and **are** particularly useful **as** components **of a multimodal analgesic regimen**

by producing analgesia through a different mechanism from that of opioids or local anesthetics. Few NSAIDS that are commonly used includes Diclofenac (100 mg per oral (PO)), Ketorolac (10 mg PO), Rofecoxib (50 mg PO), Ibuprofen (600 mg PO), Acetaminophen (1000 mg PO). KETAMINE HYDROCHLORIDE: Perioperative subanesthetic doses of ketamine reduce rescue analgesic requirements or pain intensity. It reduces

5024**-hour PCA morphine consumption and postoperative nausea or vomiting** and had minimal **adverse effects.**

Ketamine has also been administered epidurally and intrathecally, but racemic mixtures of ketamine have been found to be neurotoxic and therefore the use of neuraxial ketamine is discouraged. REGIONAL ANALGESIA TECHNIQUES: The analgesia provided by epidural and peripheral techniques is superior to that with systemic opioids and use of these techniques may even reduce morbidity and mortality. It includes ‣ Local anesthetic infiltration ‣ Nerve blocks ‣ Peripheral or plexus block ‣ Epidural – single shot, continous infusion, patient controlled epidural anesthesia ‣ Intrathecal – single shot, continous infusion.

11**DOSING OF** COMMON **NEURAXIAL** OPIOIDS: **DRUG Intrathecal single Epidural single Epidural infusion** dose dose **Fentanyl 5-25**µg **50-100**µg **25-100**µg **/hr Sufentanil 2-10**µg **10-50**µg **10-20**µg **/hr Morphine 0.1-0.3 mg 1-5 mg 0.1-1 mg/hr**

Pethidine

11**10-30 mg 20-60 mg 10-60 mg/hr**

Table 12 showing dosage of common neuraxial opioid Administration of

10**a single dose of opioid may**

be efficacious as a sole or adjuvant analgesic agent when administered intrathecally or epidurally.

10**The site of analgesic action for hydrophilic opioids is spinal.** A single bolus **of**

epidural

14**fentanyl may be administered to provide rapid**

14**postoperative analgesia,** however **diluting the epidural dose of fentanyl (typically 50 to 100**µg**) in at least 10 mL of normal saline**

is suggested to decrease the

14**onset and prolong** the duration **of analgesia, possibly as a result of an increase in initial spread and diffusion of**

the lipophilic opioid (11) Single-dose epidural morphine is effective for postoperative analgesia and may decrease postoperative patient morbidity in selected patients but is associated with following adverse effects. ADVERSE EFFECTS: ? Hypotension ? Nausea and vomiting ? Pruritus ? Respiratory depression ? Urinary retention ? Mental state changes ? Central nervous system excitation ? Herpes labialis reactivation ? Ocular dysfunction ? Gastrointestinal dysfunction. CONTINUOUS EPIDURAL ANESTHESIA & ANALGESIA: Analgesia delivered through an indwelling epidural catheter

2**is a safe and effective method for** management of acute **postoperative pain.**

Postoperative epidural analgesia can provide analgesia superior to that with systemic opioids

10**Insertion of the epidural catheter congruent to the incisional dermatome results in**

35**optimal postoperative epidural analgesia by infusing analgesic agents to the appropriate incisional dermatomes, providing superior analgesia, minimizing side effects**

(e.g., lower extremity motor block and urinary retention), and decreasing morbidity. Combination of opioid with local anaesthetic ,opioid,or local anaesthetic alone can be used for infusion.

10**PATIENT CONTROLLED EPIDURAL ANALGESIA (PCEA)** . PCEA allows individualization **of**

postoperative analgesic

26**requirements and may have several advantages over** continous epidural infusion, **including**

lower drug use and greater patient satisfaction. Lockout Continous rate Demand dose interval Analgesic solution ml/hr ml ml/min 0.05%Bupivacaine+4µg/ml Fentanyl 4 2 10 0.0625%Bupivacaine+5µg/ml Fentanyl 4-6 3-4 10-15 0.1%Bupivacaine+5µg/ml Fentanyl 6 2 10-15 0.2%Ropivacaine+5µg/ml Fentanyl 5 2 20 Table 13 Patient controlled epidural analgesia regimens. THORACIC PARAVERTEBRAL BLOCK:

12**Used for thoracic, breast, upper abdominal surgery and** for the **treatment of rib fracture pain.**

probable site of action include somatic and sympathetic nerve with epidural blockade.

12**Can be administered as single injection or** as continous **infusion.**

INTERPLEURAL ANALGESIA: Inferior to epidural and paravertebral analgesia for control of postoperative pain, preservation of lung function after thoracotomy. INTRA ARTICULAR ANALGESIA: Local peripheral administration of opioids (e.g intra-articular injection after knee surgery) may provide analgesia for

28**up to** 24 **hours after surgery and** decrease **the incidence of chronic pain.**

Peripheral opioid receptors are found on the peripheral terminals of primary afferent nerves and are upregulated during inflammation of peripheral tissues. OTHER TECHNIQUES: TENS(transcutaneous electrical nerve stimulation), acupuncture and psychological approaches. REVIEW OF LITERATURE: 1. Youn yi jo et al (13) compared outcomes of epidural ropivacaine 0.25% and epidural ropivacaine 0.25% with dexamethasone 5 mg in patients undergoing radical subtotal gastrectomy.He compared VAS scores and rescue analgesic requirements among these group of patients and concluded that VAS scores and

rescue analgesic requirements were less in dexamethasone treated group. 2. Farshad M Ahadian et al (14) in his study

> 33**compared the efficacy of three** different **doses(** 4 **mg,** 8 **mg,**

12mg) of transforaminal epidural dexamethasone in relieving radicular pain.He measured the outcomes in terms of VAS scores and subject satisfaction scale.It showed that improvement in radicular pain with no difference in efficacy of different doses of dexamethasone. 3. Wang et al (15) compared the effect of epidural dexamethasone in relieving post epidural backache in patients undergoing hemorrhoidectomy. In the study

> 24**group I patients received 25** cc **of 2%** lignocaine **with**

1 cc normal saline.

> 24**Group II patients received 25** cc **of 2%** lignocaine **with**

5 mg dexamethasone. He found decreased

> 24**severity of backache in group II patients.**

4. Thomas et al (16) evaluated the efficacy of epidural dexamethasone in reducing post operative analgesic requirements following laprascopic cholecystetcomy. In that study group I patients received IV dexamethasone 5 mg and 8 cc of 0.25% bupivacaine epidurally. Group II patients received IV normal saline 2 cc with 8 cc of 0.25% bupivacaine and dexamethasone epidurally. He concluded in the study that group II patients receiving

> 47**epidural dexamethasone 5 mg** had **effective** post operative **pain** relief **and systemic opioid requirements following** laprascopic **cholecystectomy.**

5. Jehan et al (17) studied the effect of preoperative epidural dexamethasone and magnesium sulphate in patients undergoing abdominal surgeries. In the study, group I patients received 12cc of 0.5% bupivacaine with morphine 2 mg and magnesium sulphate 50mg epidurally. Group II patients received 12 cc of 0.5%bupivacaine with morphine 2 mg and dexamethasone 6 mg epidurally. He concluded that with co administration of magnesium sulphate 50 mg or dexamethasone 6 mg as a single dose in preoperative period was associated with less postoperative narcotic consumption and VAS scores. 6. W.Neill et al (18) studied the effects of epidural methyl prednisolone 40 mg and morphine 5mg along with control group having normal saline in patients undergoing surgery for spinal stenosis. He found that the

> 2**postoperative analgesic requirement was** less **in group**

of patients receiving epidural morphine or methylprednisolone or combination of both. 7. Atsuhiro Kikuchi

> 2**et al** 19) **studied the effect of**

intrathecal and epidural methyl prednisolone in relieving the severity of

> 2**pain due to post herpetic neuralgia.**

> 53**Group I patients received** 40 **mg of**

methylprednisolone epidurally and

> 53**group II patients received** 40 **mg of**

methylprednisolone intrathecally. He concluded that pain severity was less in patients receiving intrathecal methylprednisolone due to decreased inflammatory reaction in CSF. 8. Saeid Abrishamkar et al (20)

studied the effect of epidural methylprednisolone 40 mg and local anesthetic (1 cc of 0.5% bupivacaine) impregnated in adipose tissue in relieving low back pain and radicular pain in lumbar disc surgery. He found that combination of methylprednisolone and local anaesthetic increased the duration of pain free interval. 9. Park CH (21) compared the effects of transforaminal injection of dexamethasone 7.5 mg and triamcinolone 40 mg in patients with lumbar disc herniation and found that triamcinolone is more effective in relieving lumbar radiculopathy than dexamethasone. 10. Hudan et al (22) compared the pain relief in patients with lumbar canal stenosis by epidural administration of methylprednisolone

> 4680 mg along with 0.125% bupivacaine and

triamcinolone

> 4680 mg with 0.125% bupivacaine

epidurally. He found better pain relief in patients receiving epidural methylprednisolone. 11. Khafagy et al (23) studied the effect of epidural dexamethasone in patients undergoing lower abdominal surgeries. In that study group I patients received epidural 10cc of 0.25% bupivacaine and fentanyl 50µg

> 24epidurallly and group II patients received 10cc of 0.25 bupivacaine with

dexamethasone 4 mg. He found that addition of epidural dexamethasone improved postoperative pain relief and decreased analgesic requirement. 12. Guilfoyle MR (24) studied the effect of epidural fentanyl in patients undergoing surgery for lumbar canal stenosis. In the study group I patients received normal saline epidurally

> 2at the end of surgery and group II patients received

epidural fentanyl 100 µg .

> 2Postoperative pain relief was compared with

VAS scores which showed

> 2effective post operative analgesia in group of patients

receiving bolus epidural fentanyl. 13. Ganesh A et al (25) studied the effects of epidural fentanyl infusion for post operative analgesia in infants undergoing thoracotomy . One group of patients received epidural infusion of 0.1 % bupivacaine and other group received epidural infusion of 0.1% bupivacaine with fentanyl 2µg / ml . He concluded that there was improved analgesia in group receiving fentanyl infusion with better pain scores and less rescue analgesic requirements with nalbuphine. 14. Szabova A et al (26) - postoperative epidural butorphanol / bupivacaine with the epidural analgesic infusion fentanyl / bupivacaine in children. Epidural fentanyl provided similar analgesia to epidural butarphanol after urological procedures in children, but butorphanol caused less pruritus than fentanyl. Epidural analgesia with butorphanol / bupivacaine is effective than epidural fentanyl / bupivacaine in children undergoing urological procedures. 15. Marcelo Soares Privado (27) compared the effect of epidural versus intravenous fentanyl in patients undergoing orthopaedic procedure. Group I patients received 100µg fentanyl epidurally and group II patients received 100µg fentanyl intravenously. The study outcome was less need of supplementary analgesia with tenoxicam in group I patients receiving epidural fentanyl.

> 8AIM OF THE STUDY To compare the efficacy of epidural

dexamethasone versus fentanyl on post operative analgesia

> 8MATERIALS AND METHOD: After getting Ethical committee approval

from Goverment Kilpauk Medical College Hospital. Chennai ,60

> 17patients undergoing elective hernioplasty were enrolled in the study . We conducted the

study in adult male patients aged between 25 – 45 years belonging to

2**ASA Physical status I and II**

under epidural anesthesia. STUDY DESIGN: Double blinded randomized prospective study. INCLUSION CRITERIA: ? Adult male

17**patients aged** 25 – **45 years ? ASA** physical status **I & II**

? For uncomplicated inguinal hernia surgery EXCLUSION CRITERIA : ? Patient unwilling for the procedure ? Obese ? Hypertension ? Diabetes mellitus ? History of peptic ulcer disease ? Those

5**received corticosteroids or** immune suppressive **drugs in the last 6 months**

? Those with contraindications to steroids ? Patients on anticoagulants ? Patchy or inadequate blockade RANDOMIZATION: ? Patients

17**were randomly allocated into one of the three groups** (20 patients per **group)** by lotting method. ? **Group**

1: Patients receiving 11 cc of

2**0.5 % bupivacaine plus normal saline**

1 cc epidurally. ? Group 2: Patients receiving 11 cc of 0.5 % bupivacaine plus 50 µg fentanyl epidurally. ? Group 3: Patients receiving 11 cc of 0.5 % bupivacaine plus 4 mg preservative free dexamethasone epidurally. All patients received a total volume of 15 ml of study drug including 3 ml of test dose. The level of blockade was then noted. METHOD OF BLINDING: Patients and the person performing the epidural technique was unaware of the epidural drug composition. The drug solution was prepared by an anaesthesiologist assistant in the operating room. CONDUCT OF STUDY: In the pre anesthetic visit, study plan was explained in detail to all the patients. All required basal investigations were done and assessed under ASA I or II under epidural anesthesia. Written informed consent obtained after explaining the study in their own langage. After getting informed consent, patient was prepared for the surgery with fasting period of 8 hours. Antacid prophylaxis was given with inj. Ranitidine 50 mg IV 2 hours before surgery. Baseline vital parameters were recorded in patient waiting room. MONITORS USED: In the operating room patient was connected to five lead

38**ECG, Non Invasive Blood Pressure, Pulse Oximeter and** baseline parameters **were**

recorded. An intravenous line was established with 18 gauge venflon and preloaded with 15 ml / kg of ringer lactate. MATERIALS USED: ‣ 16 Gauge Tuohy needle ‣ 18 Gauge epidural catheter ‣ Loss of resistance syringe ‣ 10 ml syringe ‣ Local anesthetic solution (3

28**ml of 0.5 % bupivacaine with epinephrine 1**

in 2,00,000 dilution) for test dose. ‣ 0.5% bupivacaine ‣ Inj. Fentanyl ‣ Inj. Dexamethasone sodium phosphate (preservative free) ‣ 22 g needle for pin prick test TECHNIQUE: Under strict aseptic precautions with the patient in right lateral position. Local anaesthtic infiltration was given with 1 % lignocaine

31**.Epidural space was identified at L2 – L3**

space through 16

31**gauge Tuohy needle** by **loss of resistance technique.** An 18 **gauge**

38epidural catheter was inserted in L2 – L3 space and 5

cm of catheter kept inside epidural space. Test dose was given with 3

28ml of 0.5 % bupivacaine with epinephrine 1:

2,00,000 dilution via catheter before it is fixed to rule out intravascular or intrathecal placement. After confirming the epidural placement of the catheter, 12 ml of blinded study solution was given and level of blockade was noted at 5 min interval till 20 minutes. Oxygen at 4L/min via venturi mask was provided. If there was any

52hypotension (systolic blood pressure< 80 mm hg or mean aterial pressure < 60 mm hg)

Inj. Ephedrine 6mg IV was given along with intravenous fluid. If the heart rate fell below 50 / minute, Inj. Atropine 0.6 mg IV was given. The respiratory rate and type of respiration was also monitored. After the administration of study medication, the onset of analgesia and the level achieved was noted at 5 min interval. Surgery was allowed to proceed when the level of blockade was T8. Throughout the intraoperative period vitals like heart rate, systolic blood pressure,

8mean arterial pressure, oxygen saturation and respiratory rate were monitored. At the end of surgery the

level of sensory blockade was assessed then patient shifted to recovery room and observed for 2 hourand vitals were recorded and shifte to Post Anesthesia Care Unit . In the PACU, pain score was observed at 30 min, 60 min, 90 min, 180 min, & then every ½ hourly intervals upto 10hrs on a 10cm Visual analogue scale ('no pain' at 0 cm end and 'worst pain ever' at 10cm end) and for occurrence of

2side effects like nausea, vomiting, pruritus, respiratory depression, sedation and

changes in hemodynamic variables. The time since injection of drug into epidural space to the time required to obtain sensory blockade upto T8 (loss of pin prick to 22 gauge needle) was noted as onset of analgesia. The time between the onset of analgesia and return to baseline VAS of 5 was noted as the duration of analgesia . STUDY PERIOD: From onset of epidural blockade to onset of postoperative pain with VAS > 5. RESCUE ANALGESIA IN THE POSTOPERATIVE PERIOD: When the VAS score was more than 5 or when the patients complained of pain, Since the study was concluded Inj. Diclofenac 50mg was given intramuscularly. The patients were followed for a period of 24 hours in PACU for any occurrence of nausea, vomiting, sedation, pruritus, respiratory depression (RR<10/min), and parameters like duration of analgesia, hemodynamic variables etc were noted. Statistical analysis was done on collected data. Analysis of variances (ANOVA) was used for comparison of mean values between more than two groups. Posthoc test was used to find any significance between the individual groups. VISUAL ANALOGUE SCALE: " Please make a mark on this line that

32describes how much pain you are having" No
0___1___2___3___4___5___6___7___8___9___10 Worst pain pain

0- No nausea/vomiting 1- Nausea 2- Vomiting 0 - No pruritus 1 – pruritus Bradycardia HR < 50 / min 0 – No bradycardia 1 – presence o bradycardia Respiratory depression RR < 10 / minute 0 – no respiratory depression 1 – presence of respiratory depression Desaturation Spo2 < 95 % 0 – no desaturation 1 – presence of desaturation Hypotension

49Systolic blood pressure < 80 mm hg Mean arterial pressure < 60 mm hg

VISUAL ANALOGUE SCALE A

3Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured (example -the

amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain).From the patient's perspective this spectrum appears continuous and their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised. Operationally a VAS is usually a horizontal line, 10cm / 100 mm in length, anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in centimetres / millimetres from the left hand end of the line to the point that the patient marks.

OBSERVATIONS & RESULTS: As per the study methodology the data of 60 male patients aged 25 – 45 years belonging to

8ASA I & II undergoing elective hernioplasty were included in the study

.The demographic data was analysed and it was found to have statistically no significant difference in parameters such as age, height, weight, ASA status. S.no

27parameter Group 1 Group 2 Group 3 p value (NS) (FENTANYL) (DEXA) 1.

Age(yr) 31.10 31.95 32.65 0.908 2 Weight(kg) 61.33 60.05 62.74 0.707 3. Height(cm) 159.28 160.50 159.72 0.985 Table 14 shows mean values of demographic parameters between groups AGE 33 32.5 32 31.5 age 31 30.5 30 1 2 3 Chart – 1 Age distribution between three groups The mean age of group1,

8group 2 and group 3 were

31.10, 31.95, 32.65 respectively. There was no statistically significant difference (p = 0.908) between the mean age of three groups, which shows these three

8groups were similar with respect to age. WEIGHT

63 62.5 62 61.5 61 60.5 weight 60 59.5 59 58.5 1 2 3 Chart – 2 Weight distribution (in kg) between three groups The mean weight of

2group 1, group 2 and 3

were 61.33, 60.05, 62.74 respectively.

2There was no statistically significant difference (p = 0.707) between three groups, which shows these groups

were similar with respect to weight. HEIGHT 160.6 160.4 160.2 160 159.8 159.6 159.4 159.2 159 158.8 158.6 1 2 3 height Chart – 3 Height distribution (in cm) between three groups The mean height of group 1, 2, and group 3 were 159.28, 160.50, 159.72 respectively. There is no statistically significant difference between three groups which shows they are comparable with respect to height. S.no

27parameter Group 1 Group 2 Group 3 p value

(NS)min (FENT)min (DEXA)min 1. Onset of 5.300 5.075 6.525 0.003 analgesia 2. Duration 256.05 347.25 373.00 0.000 Table 15 showing onset and duration of analgesia between groups ONSET OF ANALGESIA 7 6 5 4 ONSET 3 2 1 0 1 2 3 Chart – 4 diagram showing onset of analgesia significantly shorter in group 2 patients compared with group 1 and group 3. On comparing the mean onset of analgesia between three groups, the group 2 patients receiving fentanyl (5.075 minutes) had shorter onset of time than group 1 patients receiving normal saline (5.300 minutes) and group 3 patients receiving dexamethasone (6.525 minutes). The mean onset of analgesia among three groups Group 2 < Group 1 < Group 3 Thus

2**there was statistically significant difference in the** mean **onset of** analgesia among **the** three groups. (**p < 0.**

05). DURATION OF ANALGESIA 400 350 300 250 200 duration 150 100 50 0 1 2 3 Chart – 5 Diagram shows duration of analgesia is significantly prolonged in

41**group 2 patients compared with group 1 and** group 3 **patients.**

On comparing the mean duration of analgesia

41**among the three groups, group** 3 **patients**

receiving dexamethasone (373 minutes) had prolonged duration of analgesia than the group 2 (347.25 minutes) and group 1 patients (256.05 minutes). Order of duration of analgesia Group 3 > group 2 > group 1 Thus

8**there was statistically significant difference in** duration of analgesia **between groups.**

S.no

27**parameter Group 1 Group 2 Group 3 p value** (NS) (FENT) (DEXA) **1.**

Nausea 3.55% 20% - 0.000 2. pruritus - 15% - 0.033 3. sedation - 25% - 0.000 4. hypotension 10% 15% 20% 0.070 Table 16 shows side effects between three groups The side effects like nausea, pruritus and sedation were noted in fentanyl receiving group than other groups. These side effects were statistically significant on comparing between groups. (p < 0.05). Hypotension was noted in all groups, but the incidence of hypotension is higher in group 3 patients receiving dexamethasone than group 2 patients receiving fentanyl and group 1 patients receiving normal saline. None of the patients had bradycardia or respiratory depression. NAUSEA 20.00% 18.00% 16.00% 14.00% 12.00% 10.00% 8.00% 6.00% 4.00% 2.00% 0.00% 1 2 3 NAUSEA Chart – 6 diagram shows

43**significantly higher incidence of** nausea **in group 2 patients.**

The incidence of nausea in group 2 patients receiving fentanyl is 20 % and group 1 patients receiving normal saline is 3.5 %. There is nil incidence of nausea in group 3 patients receiving dexamethasone. This shows statistically significant incidence of nausea in fentanyl receiving group. PRURITUS 0.16 0.14 0.12 0.1 0.08 PRURITUS 0.06 0.04 0.02 0 1 2 3 Chart – 7 diagram shows significantly higher incidence of pruritus in group 2 The incidence of pruritus in patients receiving fentanyl is 15 %. The incidence of pruritus is nil patients receiving dexamethasone and normal saline. This shows statistically significant incidence of pruritus in fentanyl receiving group. SEDATION 0.25 0.2 0.15 SEDATION 0.1 0.05 0 1 2 3 Chart – 8 diagram showing significantly higher incidence of sedation in

2**group 2 The** incidence **of** sedation **was** 25 % **in group**

2 patients receiving fentanyl. There was nil

33**incidence of sedation in patients receiving**

dexamethasone and normal saline. This shows statistically significant

33**incidence of sedation in patients receiving**

fentanyl . HYPOTENSION 20% 18% 16% 14% 12% 10% HYPOTENSION 8% 6% 4% 2% 0% 1 2 3 Chart – 9 diagram shows higher incidence of hypotension in group 3. The incidence of hypotension in group 2 patients receiving dexamethasone, fentanyl, normal saline was 20 %, 15 %, 10 % respectively. This shows no statistically significant difference between three groups. DISCUSSION: The analgesic efficacy of epidurally administered

40**0.5% bupivacaine** + normal saline (**group** 1), **0.5% bupivacaine**

+ 50 µg fentanyl (group 2) and 0.5% bupivacaine + 4 mg dexamethasone (group 3) was studied. All the demographic variables like age, height, weight were comparable to each other. There is no statistically significant difference between the parameters. MEAN ONSET OF ANALGESIA : In our study the mean

2**onset of analgesia was** earlier **in group 2**

patients receiving fentanyl (5.07 minutes) than group 1 patients receiving normal saline (5.30 minutes) and group 3 dexamethasone group (6.52 minutes). This was found to be statistically significant.(

17**p < 0.05) The** onset **of analgesia was** earlier **in** the fentanyl **group**

when compared to the control group. This study confirmed that onset of action is earlier with combination of opioid and local anaesthetic than local anesthetic alone. This finding correlates with the study done by Manpreet Kaur et al who studied the effect of intrathecal bupivacaine alone and intrathecal bupivacaine along with opioids like butorphanol and sufentanil. The onset of analgesia was earlier in the control group receiving normal saline (5.3 minutes) than compared compared with group 3 receiving dexamethasone (6.52 minutes). This correlates with study of Youn Yi Joun et al who concluded that epidural administration of dexamethasone 5 mg in patients undergoing radical subtotal gastrectomy resulted in less VAS scores and rescue analgesic requirements than control groups. The onset of action of epidural dexamethasone is still unclear. MEAN DURATION OF ANALGESIA:

21**The duration of** post operative **analgesia was prolonged in group**

3 patients receiving dexamethasone (mean 373 minutes) than in group 2 patients receiving fentanyl (347 minutes) followed by control group receiving normal saline(256 minutes). The results of our study correlate with study done by Khafagy et al. In his study he concluded that epidural dexamethasone resulted in low post operative pain score and analgesic requirements and prolonged analgesic duration. Results of our study also correlate with the study of Thomas & Beevi et al who concluded that patients receiving epidural dexamethasone had less post operative VAS scores and analgesic consumption.

5**Dexamethasone had action at spinal cord level in addition to its action on the peripheral tissues after systemic absorption from epidural space.**

51**There was** statistically **significant difference in the incidence of nausea,** sedation, **and pruritus in**

group 3 patients receiving dexamethasone compared with group 2 patients receiving fentanyl and group 1 patients receiving normal saline. This correlated with the study done by Bisgaard et al who concluded that less incidence of nausea, pruritus, fatigue, overall pain following IV administration of dexamethasone 8 mg. SUMMARY: After getting ethical committee approval the study was conducted in 60 patients undergoing elective hernioplasty

2**belonging to ASA** physical status **I & II. The** data **were**

statistically analysed , compared and discussed. The conclusions obtained were summarised below: 1. . In our study the onset of analgesia was earlier in group 2 patients receiving fentanyl (5.075 min) and the onset was delayed in dexamethasone receiving group (6.525 min). 2. In our study the duration of analgesia was prolonged in group 3 patients receiving dexamethasone (373 min) when compared to group 2 patients receiving fentanyl (347.25 min). 3.

17**The incidence of nausea in group 1 was**

3.55 % and 20 % in group 2 patients receiving fentanyl. Hence

43**group 2 patients** have **higher incidence of**

nausea. 4. The incidence of pruritus in group 2 patients receiving fentanyl was 15%. 5. The incidence of sedation in group 2 patients receiving fentanyl was 25 %. 6. The incidence of hypotension was 10, 15, 20 %

40 **in group 1, 2 and 3 respectively** which **were**

comparable.. CONCLUSION: We conclude that epidural administration of dexamethasone – bupivacaine admixture resulted in better postoperative analgesia in terms of lower postoperative pain score, prolonged postoperative analgesia and patient comfort

31 **with fewer side effects when compared with the**

other two groups. We also conclude that this epidural dexamethasone resulted in prolonged postoperative analgesia without any side effects like nausea, vomiting, pruritus, sedation except hypotension in few patients.

GROUP A O.5% BUPIVACAINE + 1 CC NS

NAME	AGE	ASA	EPI SPACE	CATHETER LENGTH	VOLUME OF LA	ONSET OF ANALGESIA	PEAK ONSET	LEVEL ACHIEVED	BROMAGE SCALE	POST OP SENSORY LEVEL	VAS @ 30 MINUTE	VAS @ 1 HOUR	VAS @ 1 1/2 HR	VAS @ 2 HOURS	VAS @ 2 1/2 HR	VAS @ 3 HOUR
KANNAN	35	I	L2-L3	6 CM	11 CC	5 MIN	9 MIN	T6	I	T 10	0	0	1	1	1	3
CHINNAPAN	29	I	L2-L3	6 CM	11 CC	4 MIN 30 SEC	8 MIN	T6	I	T 10	0	0	1	2	2	2
THANGAMAN	25	I	L2-L3	5 CM	11 CC	6 MIN	MIN 30 SEC	T6	I	T8	0	0	0	1	1	1
ARUN	25	I	L2-L3	6 CM	11 CC	4 MIN	7 MIN	T6	II	T10	0	0	1	1	2	2
GOVINDRAJAN	32	I	L2-L3	6 CM	11 CC	MIN 30 SEC	8MIN	T6	I	T10	0	0	2	2	2	3
ARUNGIRI	36	I	L2-L3	6 CM	11 CC	7 MIN	MIN 30 SEC	T6	I	T10	0	0	1	1	2	2
KATHIRVEL	30	I	L2-L3	6 CM	11 CC	5 1/2 MIN	10 MIN	T6	I	T10	0	0	1	1	2	2
ULAGAPPA	37	I	L2-L3	6 CM	11 CC	4 MIN	8 MIN	T6	II	T 10	0	0	2	2	3	3
SANTOSH	31	I	L2-L3	6 CM	11 CC	6 MIN	9 MIN	T6	I	T10	0	0	1	2	2	2
KUMARAN	29	I	L2-L3	6 CM	11 CC	5 MIN	MIN 30 SEC	T6	I	T8	0	0	1	1	2	2
MOHANRA	26	I	L2-L3	6 CM	11 CC	3 MIN	7 MIN	T6	I	T10	0	0	2	2	2	4
SUBRAMAN	33	I	L2-L3	6 CM	11 CC	4 MIN	9 MIN	T6	I	T10	0	0	1	2	2	2
MUTHUVEL	28	I	L2-L3	6 CM	11 CC	5 MIN	7 MIN	T6	I	T10	0	0	2	2	2	3
CHENGAPP	31	I	L3-L4	6 CM	11 CC	5 MIN	MIN 30 SEC	T6	I	T10	0	0	2	2	2	2
CHARLES	36	I	L2-L3	6 CM	11CC	7 MIN	9 MIN	T5	I	T10	0	0	1	1	2	2
DHANRAJ	27	I	L2-L3	6 CM	11 CC	4 1/2 MIN	7 MIN	T6	I	T10	0	0	0	1	2	2
SUKUMAR	40	II	L2-L3	6 CM	11 CC	5 MIN	MIN 30 SEC	T6	I	T10	0	0	2	2	2	2
JEYAKUMA	32	I	L2-L3	6 CM	11 CC	6 MIN	9 MIN	T6	I	T10	0	0	0	1	2	2
VENKETESA	28	I	L2-L3	6 CM	11 CC	5 MIN	9 MIN	T6	I	T10	0	0	2	2	2	3
THIRUMAL	33	I	L2-L3	6 CM	11 CC	MIN 30 SEC	6 MIN	T6	I	T10	0	0	2	2	2	2

GROUP B - 0.5% BUPIVACAINE + FENTANYL 50 MICROGRAM

NATRAJAN	26	I	L2-L3	6 CM	11 CC	6 MIN	10 MIN	T6	II	T10	0	0	0	1	1	2
BOOPATHY	23	I	L2-L3	5 CM	11 CC	5 MIN	MIN 30 SEC	T6	II	T8	0	0	0	1	1	1
ABBAS GAN	28	I	L2-L3	6 CM	11 CC	8 MIN	10 MIN	T6	II	T10	0	0	0	1	1	1
NEELAMEG	28	I	L2-L3	5 CM	11 CC	9 MIN	12 MIN	T6	II	T8	0	0	0	0	1	1
SENTHILKU	24	I	L2-L3	6 CM	11 CC	10 MIN	12 MIN	T6	I	T8	0	0	0	0	1	1
MURALIDA	42	II	L2-L3	6 CM	11 CC	5 MIN	8 MIN	T6	I	T10	0	0	0	0	1	1
JOTHI	40	I	L2-L3	5 CM	11 CC	MIN 30 SEC	7 MIN	T6	II	T10	0	0	0	0	1	1
SEKAR	48	II	L2-L3	5 CM	11 CC	3 1/2 MIN	6 MIN	T6	I	T10	0	0	0	0	1	1
SRINATH	29	I	L2-L3	5 CM	11 CC	MIN 30 SEC	10 MIN	T6	II	T10	0	0	0	0	0	1
RAMAN	36	I	L2-L3	6 CM	11 CC	6 MIN	9 MIN	T6	I	T8	0	0	0	1	1	1
KESAVAN	30	I	L2-L3	6 CM	11 CC	8 MIN	10 MIN	T6	I	T10	0	0	0	1	1	1
BASAVAPP	42	II	L2-L3	6 CM	11 CC	7 MIN	9 MIN	T8	I	T10	0	0	0	2	2	2
VELAVAN	30	I	L2-L3	6 CM	11 CC	MIN 30 SEC	10 MIN	T6	I	T10	0	0	0	0	2	2
RAJA	32	I	L2-L3	6 CM	11 CC	5 MIN	9 MIN	T6	I	T10	0	0	0	2	2	2
PARTHASA	28	I	L2-L3	6 CM	11 CC	7 MIN	10 MIN	T6	I	T10	0	0	0	2	2	2
KUMARESA	27	I	L2-L3	6 CM	11 CC	MIN 30 SEC	8 MIN	T6	II	T10	0	0	0	2	2	2
CHARLES	30	I	L3-L4	6 CM	11 CC	7 MIN	9 MIN	T6	I	T10	0	0	0	0	2	2
RAGAVAN	32	I	L2-L3	6 CM	11 CC	6 MIN	11 MIN	T6	I	T10	0	0	0	2	2	2
CHINNASA	28	I	L2-L3	6 CM	11 CC	6 MIN	9 MIN	T6	I	T10	0	0	0	0	2	2
ULAGANAT	36	II	L2-L3	6 CM	11 CC	8 MIN	10 MIN	T6	II	T10	0	0	0	0	2	2

GROUP C - 0.5% BUPIVACAINE + 4 MG DEXAMETHASONE

RAVINDRAI	34	I	L2-L3	6 CM	11 CC	MIN 30 SEC	6 MIN	T6	I	T8	0	0	0	0	1	2
MURUGAN	45	II	L2-L3	5 CM	11 CC	5 MIN	MIN 30 SEC	T6	I	T8	0	0	0	0	0	2
BALARAM	22	I	L2-L3	6 CM	11 CC	7 MIN	10 MIN	T6	I	T10	0	0	0	1	1	1
RAMACHAI	29	I	L2-L3	6 CM	11 CC	MIN 30 SEC	11 MIN	T8	II	T10	0	0	0	2	2	2
RAVEENDR	43	I	L2-L3	5 CM	11 CC	3 MIN	8 MIN	T6	I	T10	0	0	0	0	0	2
KUMARESA	32	I	L2-L3	6 CM	11 CC	6 MIN	8 MIN	T6	I	T10	0	0	0	0	1	
SIVAKUMA	30	I	L2-L3	6 CM	11 CC	6 MIN	8 MIN	T6	II	T8	0	0	0	0	1	2
MAHESHW	28	I	L2-L3	6 CM	11 CC	4 MIN	8 MIN	T6	I	T10	0	0	0	0	1	1
APPADURA	25	I	L2-L3	6 CM	11 CC	MIN 30 SEC	7 MIN	T6	I	T10	0	0	0	1	2	2
SIVANESAN	33	I	L2-L3	5 CM	11 CC	7 MIN	10 MIN	T8	II	T10	0	0	0	1	1	1
GIRIDARAN	32	I	L2-L3	6 CM	11 CC	6 MIN	MIN 30 SEC	T6	II	T10	0	0	0	2	2	2
BASKAR	28	I	L2-L3	6 CM	11 CC	5 MIN	10 MIN	T6	II	T10	0	0	0	2	2	3
KANI	40	II	L2-L3	6 CM	11 CC	4 MIN	7 MIN	T6	II	T10	0	0	0	0	0	2
SENTHILVE	36	I	L2-L3	6 CM	11 CC	MIN 30 SEC	9 MIN	T6	I	T8	0	0	0	2	2	2
GNANASEK	27	I	L2-L3	6 CM	11 CC	MIN 30 SEC	7 MIN	T6	I	T10	0	0	0	1	1	2
ALAGESAN	38	I	L2-L3	5 CM	11 CC	4 MIN	8 MIN	T6	I	T10	0	0	0	1	1	1
SANTHOSH	25	I	L2-L3	6 CM	11 CC	6 MIN	MIN 30 SEC	T6	II	T10	0	0	0	1	1	1
MOHANRA	30	I	L2-L3	6 CM	11 CC	8 MIN	11 MIN	T6	I	T10	0	0	0	1	1	1
SURENDRA	24	I	L2-L3	6 CM	11 CC	5 MIN	MIN 30 SE	T8	I	T10	0	0	1	2	2	2
AFSAL	32	I	L2-L3	6 CM	11 CC	MIN 30 SEC	10 MIN	T6	I	T10	0	0	0	1	2	2

VAS @	VAS @	VAS @	VAS @	VAS @	VAS @	VAS @	VAS @	VAS @	VAS @	BRADY	HYPO	NAUSEA	PRURITUS	DURATION
3 1/2 HR	4 HOURS	4 1/2 HR	5 HOUR	5 1/2 HR	6 HOUR	6 1/2 HR	7 HOUR	7 1/2 HR	8 HOUR	CARDIA	TENSION	VOMITING		OF
														ANALGESIA
3	4										+			250 MIN
3	3	4												275 MIN
2	2	3	4											300 MIN
4														210 MIN
4														240 MIN
2	3	3	4											300 MIN
3	3	4												270 MIN
4														210 MIN
3	4													220 MIN
2	3	4												260 MIN
														180 MIN
3	3	3	4											306 MIN
3	4													230 MIN
3	3	4												250 MIN
3	3	4												270 MIN
4														200 MIN
2	4										+			280 MIN
3	3	3	4											320 MIN
3	4													250 MIN
2	3	3	3	4										300 MIN

2	3	4												270 MIN
1	2	2	2	3	3	4								400 MIN
2	2	2	3	3	4									360 MIN
2	2	2	2	3	3	3	4							410 MIN
2	2	2	3	3	4								+	370 MIN
1	2	2	3	3	4									360 MIN
1	2	2	2	3	4									320 MIN
1	1	3	3	3	3	4								360 MIN
1	2	2	2	2	3	3	4							450 MIN
2	2	3	3	4							+			300 MIN
1	3	3	3	3	4									350 MIN
3	3	4	4											280 MIN
2	2	2	3	3	4								+	300 MIN
2	3	3	3	4										350 MIN
2	2	4												320 MIN
2	3	3	3	4										340 MIN
3	3	3	3	3	4									380 MIN
2	3	3	3	3	3	4					+		+	365 MIN
2	2	3	3	3	3	3	4							300 MIN
2	3	3	3	3	3	4								340 MIN

3	3	3	4								+			310 MIN
2	2	2	2	3	4	4								380 MIN
3	3	4												270 MIN
2	2	3	3	3	3	3	4							430 MIN
2	2	2	3	4										330 MIN
2	2	3	3	3	4									360 MIN
2	2	3	3	4										330 MIN
2	2	4												290 MIN
2	2	3	3	3	3	4								380 MIN
2	2	2	3	3	4									320 MIN
2	3	3	4											300 MIN
3	4	4												280 MIN
2	2	3	3	3	3	3	4							423 MIN
2	3	3	3	4										330 MIN
2	2	3	3	3	4									375 MIN
2	2	3	3	4										300 MIN
1	2	2	2	2	2	3	3	4						480 MIN
2	2	2	2	3	3	4								395 MIN
	3	3	3	3	4									360 MIN
2	3	3	4											290 MIN